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STUDIES IN THE HOME TREATMENT OF STREPTOCOCCAL DISEASE*

II. A Comparison of the Efficacy of Oral Administration of Penicillin and Intramuscular Injection of Benzathine Penicillin in the Treatment of Streptococcal Pharyngitis

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PATIENTS with streptococcal pharyngitis were formerly treated by the Home Medical Service of the Massachusetts Memorial Hospitals with a seven-day course of penicillin by mouth. However, when it became apparent that more than a third of these patients were failing to take the full prescribed course of penicillin, it was decided to change to intramuscular injections of benzathine penicillin.[1]

There have been many favorable reports in the recent literature concerning the effectiveness of a single injection of benzathine penicillin G for the treatment of infections with the beta-hemolytic streptococcus.[2-4] A single injection of 600,000 units of this repository penicillin has been reported to maintain penicillin blood levels for a period of twelve to fourteen days in the majority of patients.[2,5,6] This agent, therefore, seems to have a distinct advantage in the treatment of such infections in that it would allow the physician to institute adequate therapy on first seeing the patient without having to rely on the patient's faithfulness in taking oral medication. It would also obviate the necessity of giving two or three additional injections as with procaine penicillin.

Before the change to this long-acting penicillin was made, it was decided to compare a group of patients having streptococcal pharyngitis treated with penicillin by mouth with a similar group treated with injections of benzathine penicillin.

METHODS

Only patients with clinical evidence of pharyngitis and positive throat cultures for beta-hemolytic streptococci were included in this study.

During the period November, 1954, through January, 1955, all patients were treated with 200,000 units of buffered potassium penicillin G by mouth three times daily for seven days (total of 4,200,000 units).

During the period February, 1955, through April, 1955, all patients were treated with a single injection of benzathine penicillin.‖ Children fifteen years of age or younger received 600,000 units, whereas all patients over fifteen received 900,000 units.

There were 127 patients in the group treated with penicillin by mouth and 196 patients in the group treated with benzathine penicillin by injection. Of the total 323 patients, 276 (85.4 per cent) were fifteen years of age or younger, and 47 (14.6 per cent) were older than fifteen.

In the group treated orally one follow-up throat culture was obtained between the fourth and seventh days of therapy, and another on the tenth day (that is, three days after the discontinuance of therapy). The tenth day was chosen because it was believed that the reappearance of beta-hemolytic streptococci in cultures would more probably be due to relapse than to reinfection.

In the group receiving benzathine penicillin the first follow-up culture was obtained between the fourth and the eighth day after injection, and subsequent cultures on the fourteenth, seventeenth and

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‖Kindly supplied as Bicillin by Wyeth Laboratories, Philadelphia.

twenty-first days. Since most patients have significant blood levels for fourteen days,[2,5,6] it was hoped that the seventeenth day of the benzathine-penicillin regimen would correspond to the tenth day of the oral regimen.

Treatment was begun and the initial follow-up culture was obtained by supervised Boston University medical students who spend one month during their senior year on the Home Medical Service. All additional follow-up cultures were obtained by one of us (D. N. M. or D. G. W.).

TABLE 1. *Positive Follow-up Throat Cultures in Patients Treated with Penicillin by Mouth (600,000 Units Daily for Seven Days).*

PATIENT PERFORMANCE	NO. OF PATIENTS	PATIENTS WITH POSITIVE FOLLOW-UP CULTURES
Penicillin as prescribed	90	10(11.1%)
Less penicillin than prescribed	37	12(32.4%)
Totals	127	22(17.3%)

All throat cultures were obtained by direct vision with sterile cotton swabs, planted within one or two hours on blood-agar plates containing 5 per cent horse blood, and read within eighteen to twenty-four hours.

When follow-up cultures were obtained, the patients were carefully observed for any evidence of penicillin reaction, recurrence of streptococcal infection, or streptococcal complications. Patients receiving penicillin by mouth were questioned regarding the amount of penicillin taken. Those treated with benzathine penicillin were questioned concerning discomfort at the site of injection.

TABLE 2. *Positive Follow-up Cultures in Relation to the Number of Days Penicillin Was Taken by Mouth.*

NO. OF DAYS PENICILLIN TAKEN	NO. OF PATIENTS	PATIENTS WITH POSITIVE FOLLOW-UP CULTURES
7	90	10(11.1%)
5-7	17	4(23.5%)
<5	20	8(40.0%)
<4	8	6(75.0%)

RESULTS

Group Receiving Penicillin by Mouth

Of the 127 patients in this group (Table 1) 22, or 17.3 per cent, had positive follow-up cultures for beta-hemolytic streptococci. Among the 90 patients who stated that they took the prescribed course of penicillin, there were 10, or 11.1 per cent, positive follow-up cultures, whereas among the 37 patients who admitted to taking less than the prescribed amount, there were 12, or 32.4 per cent, whose follow-up cultures were positive, a statistically significant difference ($P < 0.01$).*

The percentage of positive follow-up cultures varied inversely with the number of days the patient took the medication (Table 2).

Only 1 positive follow-up culture occurred between the fourth and seventh days in the group taking the prescribed amount of penicillin, whereas 6 positive follow-up cultures occurred during this time among the 37 patients taking the drug improperly. On the tenth day 10 positive follow-up cultures occurred among 90 patients taking the penicillin as prescribed, and 11 among 37 patients taking less than the prescribed amount. Results of follow-up cultures in relation to the day obtained are shown in Table 3.

TABLE 3. *Positive Follow-up Throat Cultures in Relation to the Day Culture Was Obtained.*

DAY CULTURE OBTAINED*	NO. OF PATIENTS	PATIENTS WITH POSITIVE CULTURES
All patients:		
1	127	127(100.0%)
4-7	127	7(5.5%)
10	125†	21(16.8%)
Patients taking penicillin as prescribed:		
1	90	90(100.0%)
4-7	90	1(1.1%)
10	90	10(11.1%)

*Penicillin started on day 1.
†Two patients could not be found for 10th-day follow-up culture.

It is of interest that no clinical relapse of pharyngitis was noted in any of this group of patients followed for ten days. However, 1 patient who took the penicillin for only one day did not recover from his pharyngitis and was given penicillin intramuscularly. It is possible that some of these patients suffered clinical relapses several days after the final follow-up study, but it is believed that most of them would have called the Home Medical Service again if this had occurred. Table 4 gives a summary of the data obtained in patients who had bacteriologic recurrences.

Group Receiving Benzathine Penicillin by Injection

There were 196 cases treated with benzathine penicillin. Four patients were included in the study twice during this three-month period, intervals of twelve, nine, four and three weeks elapsing between the two infections. The last patient was the only one treated with benzathine penicillin who suffered what may have been a clinical relapse during the three-week follow-up period. This three-year-old girl had a temperature of 102°F. twenty days after

*Values for P were obtained by the chi-square method using a four-fold contingency table.

injection; beta-hemolytic streptococci were found again on throat culture.

Among the 195 patients on whom follow-up throat cultures were obtained, 11 (5.6 per cent) had positive cultures. There were 1.6 per cent positive cultures four to eight days after treatment, 0.6 per cent after fourteen days, 3.2 per cent after seventeen days, and 4.4 per cent after twenty-one days (Table 5). The discrepancy in the total number of cultures obtained on any given day and the total number of patients in the study is due to 9 patients who could not be followed for the complete period of three weeks for various reasons* and the occasional situation in which the patient could not be reached for 1 or more of the follow-up cultures.

TABLE 4. *Summary of Data on Patients Treated with Penicillin by Mouth Who Had Bacteriologic Recurrences.*

PATIENT	AGE	NO. OF DAYS PENICILLIN TAKEN	DAY OF FOLLOW-UP CULTURE	REMARKS*
	yr.			
R.W.	3	7	7, 10†	Otitis media & meas'es
D.H.	4	1	7,† 9†	Persistent pharyngitis & fever
B.S.	46	7	7, 10†	
J.H.	6	7	7, 10†	
M.R.	10	6⅔	7, 10†	
C.C.	3	3⅓	7,† 10†	Scarlet fever
K.C.	4	3⅓	7, 10†	Scarlet fever
R.B.	22	2⅔	7,† 10†	
A.M.	7	7	7, 10†	
E.E.	5	7	7, 10†	
R.R.	8	7	7, 10†	
P.G.	5	7	7, 10†	
R.M.	3	3	7,† 10†	
D.S.	3	1⅓	7, 10†	
R.H.	9	7	7,† 10†	
P.G.	3	6	7,† 10†	
C.P.	6	6	7, 10†	Otitis media
W.B.	6	4	7, 10†	
D.B.	4	7	7, 10†	Scarlet fever
E.A.	4	4	7, 10†	
R.T.	3	7	7, 10†	
C.R.	25	3⅓	7,† 10	

*Diagnoses in addition to pharyngitis listed here, as well as any clinical relapse, complication or failure to respond.

†Culture positive for beta-hemolytic streptococci.

*Two patients had negative cultures on the fifth and seventh days after treatment and were then admitted to the hospital for tonsillectomy. Two patients had negative cultures five days after treatment and were subsequently admitted to the hospital because of symptoms suggestive of acute rheumatic fever (both are described in detail below in the section on penicillin reactions). Two patients had negative cultures three days and seven days after treatment and then moved out of the area covered by the Home Medical Service. One patient with a negative culture on the seventh day had a temperature elevation to 104°F. on the following day; she was taken to an outpatient department and received additional penicillin intramuscularly. One patient had a negative culture six days after treatment and refused further cultures. One patient called a private doctor because of persistence of fever and sore throat on the day after treatment.

No patient failed to have a clinical response to benzathine penicillin within forty-eight hours, and the majority responded within twenty-four hours. Two patients had moderate injection of the pharynx accompanying bacteriologic recurrence; 1 of these also had antral sinusitis.

There were 2 patients who had positive cultures on the fourth and sixth days respectively after treatment, the remaining 3 follow-up cultures being negative. Both had only a rare colony of beta-hemolytic streptococci on the cultures. This accounts for the fact that there were 3 patients with positive follow-up cultures four to eight days after treatment and only 1 with a positive culture at the end of two weeks. A summary of the data concerning the patients with bacteriologic recurrences is presented in Table 6.

TABLE 5. *Positive Follow-up Throat Cultures in Patients Treated with Benzathine Penicillin in Relation to the Day Culture Was Obtained.*

DAY CULTURE WAS OBTAINED*	NO. OF CULTURES	PATIENTS WITH POSITIVE CULTURES
1	196	196(100.0%)
4-8	186	3(1.6%)
14	182	1(0.6%)
17	185	6(3.2%)
21	183	8(4.4%)
Total patients with follow-up cultures	195†	11(5.6%)

*Benzathine penicillin administered on day 1.

†One patient had no follow-up cultures.

TABLE 6. *Summary of Data on Patients Treated with Benzathine Penicillin Who Had Bacteriologic Recurrences.*

PATIENT	AGE	DOSAGE OF BENZATHINE PENICILLIN	DAY OF FOLLOW-UP CULTURE				REMARKS*
	yr.	*units*					
V.C.	11	600,000	—,	13,	16,†	20	Otitis media
F.F.	12	600,000	7,†	14,†	17,	21†	
C.F.	7	600,000	8,	15,	17,†	21†	Moderate injection of pharynx
J.M.	15	600,000	6,	—,	18,	21†	
C.D.	8	600,000	6,†	14,	17,	21	
J.G.	30	900,000	4,	15,	17,†	21†	Sinusitis & moderate injection of pharynx
F.J.	20	900,000	4,	15,	17,†	21†	
J.M.	2	600,000	7,	14,	17,†	21†	
S.K.	6	600,000	7,	14,	17,	20†	Temperature of 102°F. on 20th day
A.A.	8	600,000	4,†	14,	17,	21	
K.B.	9	600,000	5,	14,	17,†	21†	

*Diagnoses in addition to pharyngitis listed here, as well as any clinical relapse, complication or failure to respond.

†Culture positive for beta-hemolytic streptococci.

Comparison of Two Groups

The comparability of the patients is indicated by the age, sex, race, presence of tonsils, and initial throat-culture results in the two groups (Table 7). It was not possible to select the patients at random for this study so that a significant bias exists in that oral treatment with penicillin was studied during the months of November, December and January, whereas treatment with benzathine penicillin was studied during the months of February, March and April. The prevalence of streptococcal disease was higher during the latter three months, as indicated by the number of patients suitable for study during each period. There was a higher percentage of nonwhite patients and patients with tonsils in the group treated orally, but there was no evidence in this study that either of these factors played a significant part in influencing the culture results.

TABLE 7. *Comparable Data in the Two Groups.*

DATUM	PATIENTS RECEIVING PENICILLIN BY MOUTH		PATIENTS RECEIVING BENZATHINE PENICILLIN	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
Patients <15 yr. of age	110	86.6	166	84.6
Female patients	67	53.8	100	51.0
Nonwhite patients	67	53.8	75	38.2
Patients with tonsils	113	91.1	163	84.0
Patients with initially positive throat culture	127	100.0	196	100.0
Months of treatment	November-January		February-April	
Total patients in study	127		196	

TABLE 8. *Comparison of Results of Follow-up Culture between Patients Receiving Penicillin by Mouth and Benzathine Penicillin.*

GROUP	NO. OF PATIENTS	NO. OF PATIENTS WITH POSITIVE FOLLOW-UP CULTURES	PERCENTAGE
Treatment with penicillin by mouth	127	22	17.3
Treatment with benzathine penicillin	195	11	5.6

The efficacy of treatment with the two methods is compared in Table 8, which shows that 17.3 per cent of the patients receiving penicillin by mouth and only 5.6 per cent of those treated with benzathine penicillin by injection had positive follow-up cultures, a highly significant difference ($P<0.001$). This difference is even more striking when it is considered that in the former group only 2 follow-up cultures were obtained over a ten-day period, whereas in the latter 4 follow-up cultures were obtained over a twenty-one-day period.

When cultures obtained on the tenth day in the group receiving oral treatment are compared with those obtained on the seventeenth day in the group in which benzathine penicillin was given by injection (assuming each to be approximately three days after disappearance of significant levels of penicillin from the blood), there were 16.8 per cent positive cultures among the former and only 3.2 per cent positive cultures among the latter, again a highly significant difference ($P<0.001$). If only patients taking the prescribed amount of penicillin by mouth are included, there were 11.1 per cent positive cultures in this group — a difference still considered significant ($P<0.02$).

In the evaluation of the over-all effectiveness of the two types of therapy, it is more realistic to include all patients in the group treated by mouth, regardless of whether or not they received the full course of penicillin, since this may give a better total picture of therapy by this method.

Household Contacts

During the six-month period of this study, throat cultures were obtained on 450 available household contacts. One hundred and twenty-five, or 27.8 per cent, of these were positive for beta-hemolytic streptococci. All contacts who had positive cultures were treated with therapeutic doses of penicillin. Of the 125 contacts with positive cultures, 46, or 38.4 per cent, had symptoms and were classified as secondary cases.

It is interesting that of the 322 contacts fifteen years of age or younger, 112 (34.8 per cent) had positive cultures; of the 128 contacts older than fifteen, only 13, or 10.8 per cent, had positive cultures, a statistically significant difference ($P<0.01$).

Reactions

There were no observed systemic reactions in any of the 127 patients treated with penicillin by mouth.

One hundred and eighty of the patients treated with benzathine penicillin were questioned and observed concerning local discomfort at the site of injection. One hundred and twenty-five, or 69.4 per cent, of these patients stated that they had discomfort. This lasted from one to seven days, with an average of two and six-tenths days.

The discomfort consisted of pain and persistent tenderness at the site of injection that was severe enough in some children to cause limping. However, only 4 patients stated that the pain was severe enough to keep them awake at night or require analgesics. No abscess formation or objective signs of inflammation were observed. Several patients had small, nontender nodules at the site of injection that persisted for as long as three weeks.

Among all the patients treated with benzathine penicillin (196 in the culture study followed for three weeks and 302 additional patients* followed for at

*These asymptomatic contacts and patients treated for pharyngitis from whose throats beta-hemolytic streptococci were not isolated were followed for at least one week. They were observed for reactions but were not recultured.

least one week), 510 injections were given to 498 patients. Four hundred and thirty-seven of these injections contained 600,000 units given to patients fifteen years of age or younger, and 73 contained 900,000 units given to patients older than fifteen. There were only 5 patients of this entire group who were observed to have signs and symptoms suggesting the possibility of a systemic reaction to penicillin. Four of these had no rash at the time of injection, and nonspecific rashes subsequently developed several hours to eight days after injection. Another patient had a rash at the time of injection, and a different type of rash developed subsequently. The pertinent details concerning these patients are as follows:

Case 1. S. F., a 2-year-old girl, was treated with 600,000 units of benzathine penicillin for acute streptococcal pharyngitis. Approximately 6 hours after injection, a scarlatiniform eruption developed, lasting for 2 days. She had received penicillin previously.

Case 2. D. P., a 3-month-old girl, received 600,000 units of benzathine penicillin for acute pharyngitis. She manifested a fine papular nonpruritic eruption 4 hours after injection that lasted for 3 days. She had received penicillin previously.

Case 3. D. S., a 3-year-old Negro girl, received an injection of 600,000 units of benzathine penicillin for acute streptococcal pharyngitis. A fine papulovesicular pruritic eruption occurred 24 hours later and lasted for 3 days. There was no history of previous penicillin administration.

Case 4. S. M., an 8-year-old girl, had fever, a generalized morbilliform eruption, erythema multiforme and generalized arthralgia when first seen. Because of injection of the pharynx and the presence of beta-hemolytic streptococci on throat culture, she was given an injection of 600,000 units of benzathine penicillin. The morbilliform eruption subsided in 2 days, but the erythema multiforme persisted. Nine days after the injection, a third type of rash, a generalized papulovesicular pruritic eruption, developed. At that time, the white-cell count was 19,000, and the sedimentation rate was 35 mm. per hour. The symptoms strongly suggested acute rheumatic fever, and she was admitted to the Boston City Hospital. In the hospital the fever, leukocytosis and elevated sedimentation rate persisted for several days, but there was no objective evidence of carditis or arthritis. She was also found to have pediculosis. The erythema multiforme subsided several days after admission; the papulovesicular eruption became hemorrhagic and persisted for 2 weeks. It was believed that she did not have rheumatic fever and that the continuing eruption probably represented a "toxic dermatitis," penicillin and pediculosis being possible etiologic agents.

Case 5. J. P., a 13-year-old Negro, called because of a painful left knee with a history of having had pain in both knees intermittently for 4 years. He was also noted to have a mild pharyngitis, and throat culture was positive for beta-hemolytic streptococci. He was therefore treated with an injection of 600,000 units of benzathine penicillin. Eight days after injection erythema marginatum and a papulovesicular pruritic eruption developed. Because of the former rash, painful swelling of the left knee, a Grade 2 apical systolic murmur (this murmur had also been noted 4 years previously), a temperature of 99.5°F., a white-cell count of 11,000 and a sedimentation rate of 56 mm. in 1 hour, he was admitted to the Massachusetts Memorial Hospitals with a suspicion of acute rheumatic fever. In the hospital, the swelling of the left knee and the erythema marginatum subsided in 2 days. The papulovesicular eruption lasted for 6 days, and antihistamines were required for control of the itching. There was no evidence of carditis, and the diagnosis of rheumatic fever remained in doubt. An L. E.-cell preparation was negative, as were 2 skin tests for penicillin sensitivity. He had received penicillin previously. It was believed that he probably had had a penicillin reaction.

Eliminating Case 1, who probably had scarlet fever and not a penicillin reaction, there were 4 patients who possibly had penicillin reactions, a rate of occurrence of 0.8 per cent out of 510 injections of benzathine penicillin.

It is of interest that no systemic reactions were observed in patients over fifteen years of age who received 900,000 units of benzathine penicillin. However, this was a relatively small group — 73 patients.

Complications

No suppurative complications were observed in either group of patients. There were no definite cases of acute rheumatic fever among patients in the study; 2 patients with possible cases were admitted to the hospital, but the diagnosis was not established. These were Cases 4 and 5, described above. Both patients had symptoms suggestive of rheumatic fever before receiving penicillin. No cases of acute glomerulonephritis were observed.

Summary and Conclusions

It would appear from this study that, for keeping the throat free of beta-hemolytic streptococci, a single injection of benzathine penicillin is more effective (94.4 per cent of patients for twenty-one days) than a seven-day course of penicillin by mouth (82.4 per cent for ten days). Also benzathine penicillin has the advantage of being less expensive than other standard forms of therapy for streptococcal pharyngitis now in use and eliminates the problem of patient reliability in taking oral medication.

It should be borne in mind that this study reveals circumstances that develop in problems of patient management in an uncontrolled environment in which the opportunity for reinfection and relapse is most likely. The results obtained under such adverse, but nevertheless realistic, conditions indicate that effective treatment could be obtained with benzathine penicillin in approximately 95 per cent of patients.

Of 127 patients with acute pharyngitis due to the beta-hemolytic streptococcus treated at home with a seven-day course of penicillin by mouth, 22, or 17.3 per cent, had bacteriologic recurrences during a ten-day follow-up period. Of 196 patients treated at home with a single injection of benzathine penicillin, 11, or 5.6 per cent, had bacteriologic recurrences during a three-week follow-up period.

Of the patients receiving benzathine penicillin, approximately 70 per cent complained of discomfort at the site of injection for an average of two and a half days.

There were 4 possible systemic penicillin reac-

tions observed after 510 injections of benzathine penicillin, a frequency of 0.8 per cent.

It is concluded that a single injection of benzathine penicillin is effective therapy for pharyngitis due to the hemolytic streptococcus, the main advantage over penicillin by mouth being that it assures the patient of receiving the intended therapy. The observations presented here deal with a comparison of intramuscular injection of benzathine penicillin G and should not be interpreted as implying any comparison with the oral route of administration of benzathine penicillin G, which was not used.

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POSTOPERATIVE BILE-DUCT STRICTURES*

Their Etiology and Treatment

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TWENTY years ago it was possible for Eliot[1] to collect all 215 cases of postoperative biliary strictures reported in the literature here and abroad. In a painstaking and brilliant fashion he reviewed each case and made many observations that, if heeded over the intervening years, might have given improved results in the care of this difficult group of patients. In recent years, sizable series of cases have appeared from various clinics, some of them running into hundreds of patients, and it is of some concern whether or not the injury to bile ducts during the course of cholecystectomy has actually become more frequent. Removal of the gall bladder has certainly become a common procedure, performed by many occasional operators, and in point of frequency is second only to appendectomy in the field of abdominal surgery. It may be fair to state that duct stricture after cholecystectomy has not decreased in frequency over the years, in spite of advances in graduate training.

Etiology

Our interest in this problem has included investigation into the etiology of these postoperative strictures. Eighty original operative notes are available from forty-three different hospitals. Eighty-one strictures occurred after operations on the biliary tract, three after subtotal gastrectomy, and one after a porta-cava shunt procedure. Two benign strictures were found in patients who had not undergone surgery of any nature (Table 1). Gallstones were present in 89 per cent of the group subjected to cholecystectomy, and only 22 per cent of these procedures were carried out in the presence of acute inflammatory disease. It is worthy of special note that 80 per cent of the gall bladders in this group of injured or later narrowed hepatic ducts were removed in a retrograde fashion, from the cystic duct to the fundus. Sixteen per cent of the operative notes reported excessive bleeding, and in 4 cases large clamps were left in situ as the operative wound was rapidly closed. In 26 per cent of the group concomitant choledochostomy was performed, and in some of the cases this procedure may have resulted in duct in-

TABLE 1. *Biliary-Tract Strictures in 87 Cases,* 1926-1955.

TYPE OF STRICTURE	NO. OF CASES
Postoperative:	
Cholecystectomy	62
Cholecystectomy & choledochostomy	19
Gastrectomy	3
Porta-cava shunt	1
Nonoperative	2
Total	87

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jury. In 9 cases an actual injury to the hepatic or common duct was recognized, and an attempt at repair carried out (Table 2).

But is it always a hurried, inexperienced operator working through a too-small laparotomy wound, with poor anesthesia, no light and much blood? The answer, we believe, is most certainly not. Examination of the 80 available original operative notes indicates that the cause of stricture is not always due to gross errors in technic but may result from relatively minor omissions or may be due to the patient's original disease itself. Of the total of 81 postcholecystectomy strictures only 30, or 37 per cent, were due to proved injury to the duct recognized at operation or discovered by necessity at laparotomy soon after the original procedure. Mistaken anomalous ducts were tied and cut, massive hemorrhage occurred, and clamps were left in situ, or at an early subsequent operation catgut ties were removed from a severed duct, or a segment of the duct was found missing. In the remaining 63 per cent of the patients it is obvious that many ducts were unknowingly tented or compromised by inept surgery, only to give symptoms of cholangitis and jaundice months later, so that gross injury probably accounts for many more of these strictures.

TABLE 2. *Data Associated with the Original Cholecystectomy (74 Operations in 43 Hospitals).*

DATUM	NO. OF CASES
Finding:	
Gallstones	66(89%)
Acute inflammation	17(22%)
Procedure:	
Bladder removed, duct-to-fundus	43(54)* (80%)
Common duct explored	19(26%)
Hemorrhage	12(16%)
Injury recognized	9(12%)

*Operative note not clear in 20 cases.

TABLE 3. *Causes of Postoperative Stricture of the Hepatic or Common Duct (81 Cases).*

CAUSE OF STRICTURE	NO. OF PROVED CASES
Tenting or peaking of duct	6
Incision or excision of segment of duct	19
Segmental stenosis of duct due to recurrent cholecystitis or stone in duct	3
Cholecyst-choledochal fistula due to ulcerating stone	1
Periductal fibrosis due to extravasated bile or blood or to infection	?

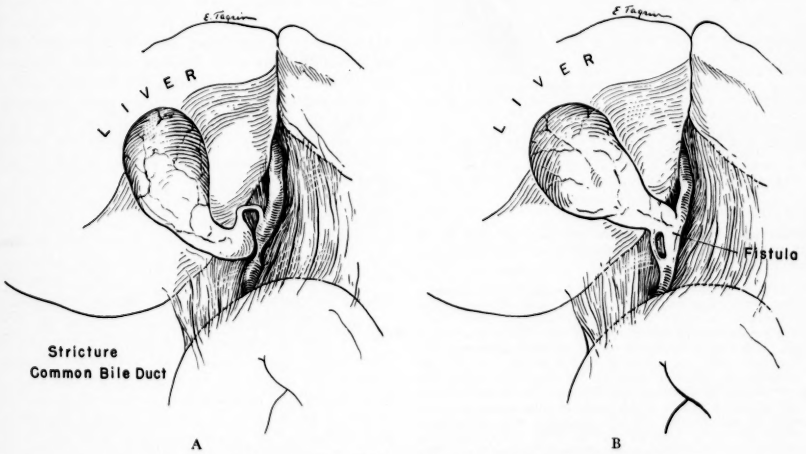

FIGURE 1. *Primary Biliary Disease As the Cause of Segmental Stenosis.*
The narrowing of the common duct (A) *is the result of recurrent cholecystitis in a prolapsed gall bladder. A case of fistula formation between the gall bladder and the duct* (B), *caused by ulceration of a stone, was encountered in this series.*

In a small but definite percentage, however, we believe that the primary disease of recurrent cholecystitis or of cholelithiasis is responsible for some narrowed ducts and that, in a second group, the events that follow cholecystectomy may produce stricture (Table 3 and Fig. 1). Infection, blood and particularly a bile collection allowed to remain about

the common duct after operation are adequate causes of late duct obstruction. Dr. Roscoe Graham reported such a stenosis of his own in 1936, and expressed the opinion that retained bile acids produce periductal edema and later fibrosis (Fig. 2). Lahey has found complete obstruction to the extrahepatic biliary radicles after nonoperative liver trauma with bile peritonitis. A case from our own hospital records lends support to the belief that bile collections should not be allowed to remain inadequately drained:

A 23-year-old mother, a typhoid-carrier suspect, had been subjected to cholecystectomy 16 years previously at the Massachusetts General Hospital. She was operated on by the senior resident at the time, and an uneventful procedure was described, as follows:

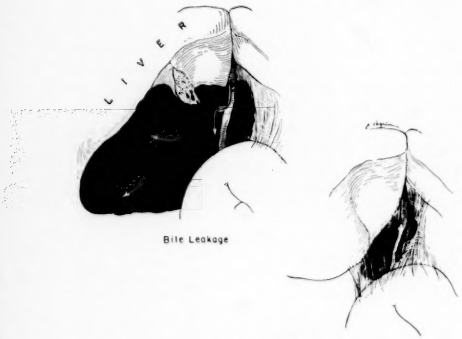

FIGURE 2. *Subhepatic Collection of Blood, Infection or Bile, Derived from the Gall-Bladder Bed, Cystic-Duct Stump or Lacerated Common Duct, Causing Periductal Edema and Late Fibrosis about All Structures in the Porta Hepatis. A diffuse duct stenosis results.*

> Under general anesthesia a right paramedian incision was made. The gall bladder was a small, fibrosed organ containing a chain of pea-sized stones. There were a few adhesions to the duodenum. The bowel was packed off, and the gall bladder freed of its adhesions. The common duct was identified and appeared normal. An attempt was made to mobilize the structures around the cystic duct and artery, but because these extended so far up under the liver this mode of attack was given up and the gall-bladder bed was distended with saline solution, producing artificial edema. The peritoneum was incised, and the organ removed from above down. The gall bladder was traced down to the cystic duct, which was clamped and cut across. A stone about the size of a marble was impacted in the ampulla. The cystic duct was not enlarged. The artery and duct were then separately secured with chromic catgut. The liver bed was closed with an atraumatic running stitch, and Morrison's pouch was drained through a stab wound. The field was dry, and the abdomen was closed in layers after the omentum had been brought up to prevent postoperative adhesions to the gall-bladder bed.
>
> After operation bile drainage was described as moderate, but it continued until the 6th day, when jaundice appeared. A brown stool was passed on this day. By the 8th postoperative day the entire upper abdomen was tender, and a diagnosis of bile leakage was made. Finger exploration via the drain site released 300 cc. of bile and some purulent material. On the 11th day the wound was opened, and a large collection of bile was found above and below the liver and in the pelvis. Drains were placed, and bile drainage continued copiously as jaundice lessened. Throughout the succeeding 3 weeks light-brown stools were passed on occasion, as there was clinical improvement. Vomiting then developed, and a mass appeared in the right upper quadrant. On the 34th day a hematoma was evacuated, and a jejunostomy established so that bile drainage might be returned to the gastrointestinal tract; 300 cc. of bile was returned daily. Stool reports thereafter, of course, continued to show bile, although previously all reported stools had had bile in them. After a 3-month hospital stay the patient was discharged with a small fistula, draining 50 to 100 cc. of bile a day.
>
> Two months later she returned for the first of 3 reconstructive procedures over a 3½-year period. She was not icteric, but when bile was withheld from the jejunostomy tube, the stools were consistently acholic. On exposure of the porta hepatis at operation, the common duct was found to be a fibrous cord. After 2 attempts at choledochodochostomy, a choledochoduodenostomy was performed, and the patient's condition has remained satisfactory for the past 12 years.

Cole[2] has expressed a similar opinion that pus or bile deposited about the common duct and inadequately drained may cause later stenosis, and estimates that as many as a third of his cases of stricture are due to nonoperative trauma of this nature. Boren and Walters[3] have suggested a much lower figure of only 5 per cent in their group of cases. It has long been accepted that free bile in the peritoneal cavity holds many acute hazards, resulting in vascular collapse and renal failure, but the later effects of local collections of bile have not been adequately emphasized. Too many of the cases in our study were allowed to drain profusely without any further immediate investigation, and have resulted in bile cysts or periductal fibrosis.

In 31 cases (39 per cent) bile drainage after operation was profuse, and it was obvious that some error in technic had been committed. Rarely was secondary drainage instituted, and when early operation was carried out, the procedure fell short of investigation of the common duct itself. We can only speculate about the events that might have occurred. Possibly, a divot of common duct had been removed in some cases. Certainly, a single cystic-duct ligature presents the hazard of slipping. Hayes and Coller[4] have recalled the presence of embryonic ducts leading directly from the liver to the gall bladder. Failure to reperitonealize the gall-bladder bed may, in an occasional case, allow excess leakage from one of these anomalous ducts.

JAUNDICE

Jaundice occurred within the first five postoperative days in 40 per cent of the cases, but again most often exploration was deferred for weeks, and as long as four months in 1 case. It is in this group that gross duct injury was most often demonstrated and a tented duct found, or catgut ties were removed from a severed common duct. The results of treatment

in this group with positive duct injury were most satisfactory, and 66 per cent of patients were relieved permanently of their obstruction by an early, single reconstruction (Table 4).

Over 50 per cent of the group manifested their jaundice at a later date — in some as the result of a previous fistula closing. In 8 such cases bile cysts were found at a secondary operation and were either drained or utilized to direct bile into the gastrointestinal tract. They were at times thought to represent accessory gall bladders. More often late jaundice indicated dense fibrosis and foreshortening of all structures about the porta hepatis, and these represented the group of patients in whom surgical relief was most difficult (Fig. 3).

Results of Therapy

It must be admitted that some of the conclusions dealing with the etiology of postoperative duct stricture are on somewhat tenuous ground. Data in the form of operative and postoperative events in a group of patients drawn from 43 different hospitals leave something to be desired. Similarly, any assessment of the results of therapy must be made guardedly. Walters and Cameron[5] and others have observed that the longer this group of patients is followed, the poorer the results. Symptoms of cholangitis may recur if biliary cirrhosis asserts itself. The longest interval before failure is that of a patient described by Williams and Smithwick.[6] This reconstruction, the first successful biliary fistula-to-duodenum anastomosis, was done in 1913 at the Massachusetts General Hospital. Twenty-eight years later mild attacks of pain with slight jaundice occurred, and in 1945, thirty-two years after the original operation, a stenosed anastomosis was found by Smithwick. A choledochoduodenostomy was re-established over a T tube. Pearse[7] has recently again reported his first choledochodochostomy over a vitallium tube reconstructed twelve years previously. Symptoms of obstruction to the flow of bile necessitated the removal of a completely bile-encrusted tube from a large common duct after this long interval. In 1 case in our own series a choledochoduodenostomy required re-exploration nineteen years later, and at this time, seven years ago, a choledochojejunostomy was successfully constructed.

Disturbing as these late recurrences are, in the group of 87 cases here reported, symptoms recurred in 82 per cent of the failures after 120 reconstructions within a year of operation. The great majority had some symptoms within months — and our result studies are based on the status of the patient two or more years after the most recent reconstruction. Results have been graded as good in patients who have had no biliary symptoms whatsoever, and as fair in those who have had occasional postprandial heaviness or distress or rare fever without jaundice. In terms of reconstructions attempted, by whatever method, it appears that the results have not been gratifying (Table 5).

Table 4. *Events after the Original Cholecystectomy (80 Cases).*

Event	No. of Cases
Profuse bile drainage	31(39%)
Immediate jaundice (2 to 5 days)	32(40%)
Delayed jaundice (1 mo. to 12 yr.)	42(53%)
Persistent fistula	6(7%)

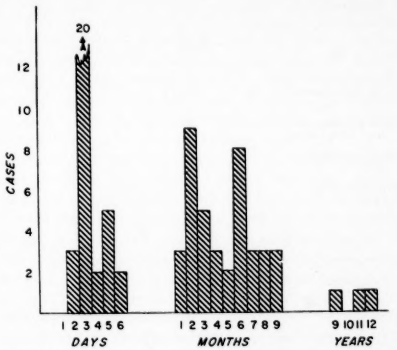

Figure 3. *Interval between Cholecystectomy and Jaundice in 74 Cases.*

The appearance of jaundice after biliary-duct injury follows a fairly definite pattern. Forty per cent of this group demonstrated jaundice within the first week of cholecystectomy, and 39 per cent drained bile profusely, only to manifest jaundice months later. In a smaller group late jaundice developed in the absence of any remarkable symptoms immediately after operation.

Five patients have been operated on within the two-year interval, too recently to allow reporting. Another 5 with injured ducts were not subjected to reconstruction, laparotomy for drainage or for choledochostomy alone being done. In 1 of these cases dilatation of a narrowed duct with insertion of a T tube was performed on three occasions, only to result in recurrent stenosis and liver failure. Simple dilatation of a stricture is to be condemned, and excision of the diseased portion of the duct with reanastomosis is essential. There were 5 operative deaths after reconstruction, a patient mortality of 6.1 per cent, or a reconstruction mortality of 4.0 per cent. Cattell[8] and Boren and Walters,[3] in large series of cases, have reported a similar mortality, and it is of some surprise that this seriously ill group of patients tolerate extensive surgery as well as they do (Tables 6 and 7).

Of the remaining 72 patients, 60 were found to have a satisfactory result two or more years after their most recent operation. If one includes the 5 operative deaths in this group, 78 per cent of these patients were restored to an essentially normal life. The shortest follow-up period is just two years, and the longest is that of a patient who had her third reconstruction performed nineteen years ago. It is accepted that some of the more recent procedures are doomed to failure with the lapse of time, but the patient results in this statistical follow-up study are much more heartening than previously indicated (Table 8). This discrepancy in results in total reconstructions (120) and total patients (77) is due to several details that have become evident in the care of these patients and have affected the results favorably in more recent years.

TABLE 5. *Results of Bile-Duct Reconstructions at the Massachusetts General Hospital (1926 - August, 1955).*

TYPE OF RECONSTRUCTION	NO. OF CASES	FAILURE	FAIR RESULT	GOOD RESULT	SATISFACTORY RESULT
		NO. OF CASES	NO. OF CASES	NO. OF CASES	
					%
Choledochodochostomy	56	24	1	31	57
Choledochojejunostomy (Roux type)	40	20	4	16	50
Choledochoduodenostomy	21	12	4	5	43
Fistuloduodenostomy	3	2	1	0	33
Totals	120*	58	10	52	
Average					52

*5 operations too recent to evaluate.

TABLE 6. *Common-Duct Reconstructions in 87 Cases (1926 - August, 1955).*

TYPE OF PROCEDURE	NO. OF OPERATIONS	NO. OF DEATHS	MORTALITY
			%
Reconstruction	125	5	4.0
Exploration	9	3	33.0
Removal of plugged tube	8	0	—
Totals	142	8	
Average			5.6

DISCUSSION

Many factors must influence the success or failure of biliary reconstruction in any patient. These include the status of the liver, the number of previous attempts at reconstruction, the extent of dissection necessary, the type of anastomosis possible, the type of splint used and the period in which the splint is left in place. The immediate factor of greatest importance is the status of the patient's liver. All are impaired, as indicated by jaundice, and all require careful evaluation by various liver-function tests, including determinations of protein, albumin-globulin ratio, prothrombin time, cephalin flocculation and alkaline phosphatase. Of the 5 deaths that followed reconstructive procedures, 2 are directly attributable to liver insufficiency. Ten patients subsequently died, presumably of recurrent cholangitis and eventual liver failure, up to seven years after the final reconstruction, and these cases are classified as failures. Cole[2] has emphasized the difficulty in distinguishing duct obstruction from hepatic damage in the form of biliary cirrhosis and hepatomegaly.

The statistical likelihood of success or failure is probably related to the number of attempts at reconstruction in any patient although this point is difficult to assess in a small series of cases. A satisfactory result was obtained in 44 per cent of reconstructions after a single try, leaving 32 patients in whom a second attempt was made. Success or failure thereafter was variable. Of 9 patients subjected to 4 operations or more, 50 per cent had a successful result after the fourth attempt; and 1 patient, after 6 reconstructions over a four-year period, has been entirely well for eight and a half years. In general, however, the greater the number of operative procedures and the more extensive the dissection, the less likelihood of

TABLE 7. *Types of Reconstruction in 87 Cases (1926 - August, 1955).*

TYPE OF PROCEDURE	NO. OF CASES	MORTALITY
		%
Choledochodochostomy	60	5.0
Choledochojejunostomy — Roux type	40	2.5
Choledochoduodenostomy	22	4.5
External fistuloduodenostomy	3	0.0
Total	125	
Average		4.0

TABLE 8. *Results of Bile-Duct Reconstruction in 77 Patients.**

RESULT	NO. OF CASES
Failure:	
Operative death	5
Later death from biliary disease	10
Later treatment elsewhere	2
Total	17(22%)
Satisfactory result:	
Fair	9
Good	51
Total	60(78%)

*5 operations too recent to evaluate.

success; we believe that an early, bile-tight reconstruction at the first attempt offers the greatest chance for permanent cure.

Great has been the discussion regarding the type of operation that one should undertake. Eliot,[1] twenty years ago, favored reconstruction of the duct itself even though there was a discrepancy in size between the upper and lower ends. Over the years, Walton,[9] Cole,[2] Cattell[10] and others have come to the same conclusion. Boren and Walters[3] continue to advocate choledochoduodenostomy as a less taxing procedure, giving better results in their series. Although most of the earlier cases at the Massachusetts General Hospital were treated by choledochoduodenostomy from the start, and our longest survival (nineteen years) was in a case so constructed, the tendency has been to search for the lower end of the common duct, at least initially, and perform a choledochodochostomy over a prosthesis. Twenty-four of the 38 initial operations performed in this manner (63 per cent) resulted in a successful outcome. Subsequent procedures, after initial failure, are often done in the face of severe scarring requiring considerable dissection, and the lower end of the common duct cannot always be found. As mentioned above, we believe that duct stricture is often initiated and may result entirely from the structures about the duct itself and particularly about the point of the actual anastomosis. Extensive dissection invites fibrosis and contracture, and it is probably better in the face of initial failure to utilize virginal tissue such as is provided by a limb of jejunum in Roux Y fashion in the reconstruction described in 1945 by Allen.[11] In general, operations that have been done after an initial failure or two have been of this type, splinted by vitallium or polyethylene tubing. Regurgitation of intestinal contents into the biliary radicles has not been a problem so long as the enteroenterostomy lies 31 to 36 cm. below the choledochojejunostomy. The establishment of valves in this limb is unnecessary. Most observers now agree that cholangitis subsequent to biliary-tract anastomoses is due to stenosis at the suture line, rather than to the regurgitation of intestinal contents into the bile ducts.

The value of a prosthesis to support the anastomosis has become fairly well established. The common duct is essentially a passive tube, and the column of fluid within it gives little support in the face of constricting scar tissue. In an occasional primary case in which little dissection is necessary and the duct is large, splinting may be unnecessary. Only 4 such cases were encountered in this series, and 2 of these gave successful results. In general, however, the use of a prosthesis is a valuable adjunct and has been widely practiced.

It has also become evident that the perfect prosthesis has yet to be found. Many prolapse because of weight or plug as a result of bile encrustation. In some of the more recent cases the type of support is determined by the number of previous failures and the type of operation performed. When choledochodochostomy is possible, at the initial or second operation, a rubber T tube of largest bore possible is used instead of vitallium or polyethylene tubing. Although rubber may favor the precipitation of bile salts, the T tube, by irrigation, can usually be kept patent for nine to fifteen months. The time necessary for the reaction about an anastomosis to subside must be variable, depending on the perfection of the anastomosis, infection and other factors relating to healing in any given patient. In general a few months is not long enough, and we are convinced that failures in our group have been due to impatience and too early removal of these tubes. Most consistent results have followed the use of a T tube for nine to fifteen months, when the great advantage of easy removal is apparent.

In the recurrent, more difficult cases, vitallium and more recently polyethylene tubing has been used. These are placed with no thought of removal, but are securely anchored with wire. Both types of tubes will become plugged, but probably less readily than rubber. Vitallium is more difficult to anchor and, because of its weight, tends to prolapse. Polyethylene has been used as the prosthesis of choice in the choledochojejunostomy group, and occasionally in the recurrent choledochodochostomy reconstructions. On 8 occasions a secondary procedure has been necessary because of fever, chills and jaundice, and a plugged tube has been removed from a widely patent anastomosis. At such a time every effort is made to disturb the tissues about the actual suture line as little as possible, and the tube can usually be slipped out from below, leaving a draining whistle-tip catheter in the duct for a few days only to prevent leakage. It is possible that in some of the more difficult cases a two-stage operation should be deliberately planned, for the results of removing a plugged tube two to five years after the original reconstruction have been uniformly good.

Summary and Conclusions

Eighty-seven benign strictures of the bile ducts are considered; 82 patients were subjected to 125 reconstructive procedures.

An inquiry into the original operation is described. The operative findings and procedure in reports from 43 different hospitals are reviewed.

A definite percentage of strictures after cholecystectomy or choledochostomy are due to the patient's primary disease and not to operative trauma.

Extravasation of bile, blood or infection, with subsequent fibrosis, is responsible for a number of strictures. Profuse bile drainage after surgery demands early operative intervention, including inspection of the biliary tree and wide drainage of the right upper quadrant.

Results of treatment are tabulated according to the type of operation performed. Seventy-eight per cent of all the patients undergoing reconstruction

now have a satisfactory result. The patient mortality is 6.1 per cent.

Factors influencing the results of treatment are discussed, including liver status, the amount of dissection necessary, the type of operation performed and the type and duration of prosthesis used.

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CONGENITAL CAPILLARY HEMANGIOMAS OF THE PAROTID GLAND*

A Lesion Characteristic of Infancy

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THE diagnostically significant fact that "vascular tumours are the characteristic tumours of the parotid gland in the first year of life"[1,2] has been omitted from many standard medical textbooks, is underemphasized in published reports dealing directly with hemangiomas of the parotid gland and appears to form no part of the average physician's information concerning parotid disease. For these reasons 3 cases of congenital capillary hemangioma of the parotid gland are added to 58 cases already reported. Table 1 summarizes the clinical data.

Table 1. *Clinical Data.*

Case No.	Age at Onset	Age at Operation	Sex	Treatment	Complication	Follow-up Result
	mo.	*mo.*				
1	4	11	F	Subtotal parotidectomy	Transient facial-nerve palsy	No recurrence in 9 mo.
2	2	3	F	Subtotal parotidectomy	None	No recurrence in 3 mo.
3	1	18	F	Subtotal parotidectomy	None	No recurrence in 3 mo.

Case Reports

Case 1.‡ A female infant was first noted to have an enlargement in the left parotid region at the age of 4 months. The lesion increased in size very slowly in succeeding weeks, and medical aid was first sought when she was 7 months of age. Physical examination at that time disclosed in the site of the left parotid gland a firm, rubbery, deep-seated mass, which was estimated to measure 2 or 3 cm. in diameter. Subsequently, the lesion appeared to enlarge much more rapidly, producing an obvious and alarming facial deformity. This enlargement was distinctly progressive. In all other respects postnatal development had been unremarkable. The infant was admitted to the hospital at the age of 11 months, when the lesion was estimated to measure 5 cm. in diameter.

This infant had been delivered vaginally without forceps after an uneventful pregnancy into a family comprising 1 female and 2 male siblings, all of whom were healthy. The mother, aged 33 years, and the father, aged 35 years, were both well. No congenital anomalies were known to exist in siblings or parents, grandparents or other close relatives. There was no history of familial telangiectasia.

Physical examination gave no evidence of disease apart from the mass occupying the site of the left parotid gland. This mass was of moderately firm consistence and resilient but was not noted to compress readily on pressure or to swell on crying. It showed no attachment to the overlying skin, which was of normal color. The regional lymph nodes were not palpably enlarged. There were no cutaneous angiomas. No funduscopic examination was recorded. No congenital anomalies were found. Routine laboratory examinations of blood and urine were unremarkable, as were radiograms of the skull.

A left-sided subtotal parotidectomy, with excision of the mass, was carried out in the face of brisk bleeding.

The specimen§ was examined in the fresh, unfixed state. It comprised 10 gm. of coarsely lobated firm and resilient tissue forming a sharply demarcated mass partly embedded in fat. It measured approximately 2.0 by 1.5 by 1.0 cm. The cut surfaces were coarsely lobated, purplish red and bloody. Its resemblance to healthy parotid gland was striking, but it appeared large for the normal parotid gland at this age, and its lobules were coarser and darker and bled more freely.

Paraffin-embedded sections were examined by hematin, phloxine and saffron stain, by van Gieson's and Mallory's connective-tissue stains, by Weigert's elastic-tissue stain, by silver impregnation for reticulum and by phosphotungstic acid hematoxylin stains. The microscopical picture was characterized in virtually all fields by almost complete replacement of the parotid acini and ducts by a tangled network of anastomosing channels, many of which contained red blood cells. These channels were lined by a single layer of spindle-shaped cells with interlacing cytoplasmic processes, and uniform, plump, ovoid nuclei containing moderately coarse chromatin and inconspicuous nucleoli. Many of these channels were of capillary size, although some had the caliber of venules. Each of these vessels showed in its walls, supporting its lining cells, a narrow membrane of collagen and reticulum, to which, in some areas, the cytoplasmic processes of the lining cells could be seen to contribute. Applied externally and also contributing to this membrane were other spindle-shaped cells with smaller compact and slender nuclei. In several fields small muscular arteries and veins

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‡Reported through the courtesy of F.H.Côté, M.D., F.R.C.S.

§O.G.H. S-54-1741.

appeared to wander at random. All these vessels were embedded in a scanty stroma composed of lightly collagenized, moderately cellular fibrous connective tissue.

In areas a few isolated clumps of parotid acini and ducts appeared, but vessels comprised the bulk of the coarse lobular structures that were observed grossly. Some of these structures in the periphery of the lesion enclosed in their borders narrow, imperfectly demarcated zones of intact acini and ducts. Still farther peripherally, there were a few small and compressed but otherwise intact lobules of parotid tissue.

Although moderate numbers of mitotic figures were observed, the uniformity of the vessel-building cells, their failure to transgress the borders of the coarse lobules in which they were arranged, the survival of few but perfectly preserved ducts and acini within the growth and the absence of invasion of fat bordering the lesion were accepted as reliable evidence that the lesion was benign. Equally important, the lesion was evidently locally removed. A histologic diagnosis of benign capillary hemangioma of the parotid gland was reached.

On the 1st postoperative day, a complete facial palsy was noted, but when the child left the hospital 3 days later she was otherwise well. No postoperative irradiation therapy was given.

Three months after operation the only evidence of residual facial-nerve damage was slight asymmetry of the mouth in smiling. There was no suggestion of a recurrent mass in the left parotid region; nor was any evidence of recurrence detected after a further lapse of 6 months. By that time facial-nerve function had fully returned.

CASE 2.* A normally developing female infant was approximately 10 weeks of age when medical attention was sought for the 1st time because of cough and fever. Physical examination disclosed a mass in the right parotid region. After some days the patient, failing to improve, was admitted to the hospital with a temperature of 101.3°F., a slight nonproductive cough and frequent pasty-yellow stools.

The infant had weighed 2.7 kg. (6 pounds) when delivered normally from a healthy 23-year-old mother. The father, aged 23 years, was also well. The state of health of the only sibling, a female, was not specified, but congenital defects were said not to exist in this sibling, in the parents or in close relatives, and a history of familial telangiectasia was denied.

Details of the physical examination of the mass in the parotid region were not recorded. No mention was made of the presence of cutaneous lesions. No funduscopic examination was recorded. No congenital anomalies were demonstrated. X-ray examination of the lung fields showed only increased bronchovascular markings. Laboratory studies of urine and blood were unremarkable.

On the 17th hospital day, after fever and cough had subsided, a right-sided subtotal parotidectomy, with excision of the mass, was performed.

The specimen† was examined after formalin fixation. It comprised 10 gm. of firm and resilient pale, reddish-gray tissue, arranged in grapelike spheroid lobules of variable size that were held loosely together by a few strands of fibrous connective tissue. It measured 2.5 by 2.0 by 1.3 cm.

Paraffin-embedded sections were examined by hematin, phloxine and saffron stain, by van Gieson's and Mallory's connective-tissue stains, by Weigert's elastic-tissue stain, by silver impregnation for reticulum and by phosphotungstic acid hematoxylin stains. A histologic picture resembling in detail that seen in Case 1 was encountered. Coarse lobular structures comprising the tumor were dissociated from one another as though pulled apart in handling, so that the margins of resection could not be accurately defined. A few lobules of healthy tissue were included in some borders of the specimen.

Postoperative recovery was uneventful, and the patient was discharged from the hospital on the 8th postoperative day without evidence of facial-nerve damage. No postoperative irradiation therapy was given.

Three months later there was no evidence of a recurrent mass in the right parotid region.

CASE 3.‡ A female infant was first noted to have a unilateral enlargement of the left parotid gland at the age of 3 weeks. This lesion grew slowly but progressively larger. Postnatal development was otherwise unremarkable. The patient entered the hospital for treatment of the parotid lesion when she was 18 months of age.

She had weighed 2.7 kg. (6 pounds) when delivered, the first of heterozygous twins, from a healthy 27-year-old mother. There were no prenatal complications or infections, and there were no placental anomalies. A twin sister was healthy, with no evidence of parotid enlargement. Two other siblings, both girls, 1 and 3 years of age, were in good health, as was the 26-year-old father. There were no known congenital anomalies or signs of hereditary telangiectasia in parents, siblings or close relatives.

Physical examination gave no evidence of disease except for the mass in the region of the left parotid gland. This was estimated to measure approximately 5.0 by 3.0 cm. It was ovoid, soft and compressible, but did not fluctuate in size on crying. The overlying skin showed bluish discoloration, but no cutaneous angiomas were demonstrable in this or other regions. No bruit could be heard over the lesion. The regional lymph nodes were not palpably enlarged. The optic fundi were unremarkable, and no congenital anomalies were found.

A subtotal parotidectomy, with excision of the mass, was carried out in spite of moderate bleeding. Postoperatively, there was no facial palsy or other complication from the operation. Recovery was uneventful. No postoperative irradiation was given.

The specimen§ was examined after formalin fixation. It comprised 8 gm. of firm and resilient, reddish-gray tissue arranged in coarse lobules, bordered in areas by fat and in areas by paler tissue arranged in smaller lobules resembling those of normal parotid glands. This specimen measured 3.5 by 3.0 by 2.0 cm.

Paraffin-embedded sections were examined by hematin, phloxine and saffron stain, by van Gieson's and by Mallory's connective-tissue stains, by Weigert's elastic-tissue stain, by silver impregnation for reticulum and by phosphotungstic acid hematoxylin stain. A histologic picture resembling in detail that seen in Cases 1 and 2 was encountered. The lesion was partly bordered by fat and by lobules of normal parotid gland, but in areas it appeared to extend to the lines of resection.

Three months after operation there was no evidence of a recurrent parotid mass.

DISCUSSION

Histologically, the parotid lesions reported here were typically benign capillary hemangiomas. All three lesions comprised relatively well differentiated mesenchymal cells building small blood vessels (Fig. 1). Progressive growth favors their inclusion among true tumors. Other reported cases have shown variable but essentially similar features. The general subject of parotid neoplasia in children was summarized by Howard et al.[2] in 1950. The literature describing parotid hemangiomas was reviewed by McFarland[3] in 1930. Glaser and his associates[4] referred to their case, reported in 1946, as a "hemangioendothelioma." Caldwell[5] distinguished his case, reported in 1952, as the first to appear in the British literature. Since this study was begun, additional cases and a review of this subject have been contributed

*Contributed from the files of the Canadian Tumour Registry of the National Cancer Institute of Canada through the courtesy of the registrar, Desmond Magner, M.D., and the contributing pathologist, P. N. Karnauchow, M.D.

†C.T.R. 1651.

‡Contributed from the files of the Canadian Tumour Registry through the courtesy of the registrar, Desmond Magner, M.D., and with the permission of D. N. Barnbrook, F.R.C.S., of Kapuskasing, Ontario, and J. B. MacKay, M.D., of Toronto, the contributing pathologist.

§C.T.R. 1718.

by Wawro and his co-workers.[6] The statistics that follow include the 3 cases reported above.

Excluded for want of data is Case 19 of McFarland's[2] review. Cavernous hemangiomas of the parotid gland reviewed by Howard et al.,[2] by McFarland[3] and by Wawro and his associates[6] are also excluded because the histologic diagnosis and other data[3] suggest a somewhat different lesion, and because the original reports are not available for evaluation. It is not unreasonable to consider that both capillary and cavernous hemangiomas of the parotid gland may be merely slightly differing manifestations of the congenital vascular dysplasias of the head and neck regions that are familiar in the form of cutaneous port-wine stains. In fact, hemangiomas of the overlying skin are a common associated lesion,[2,3,6] but capillary hemangiomas of the parotid gland have apparently not yet been recorded in association with more serious vascular anomalies such as intracranial cirsoid aneurysm, and their progressive growth seems to distinguish them from simple vascular hamartomas.

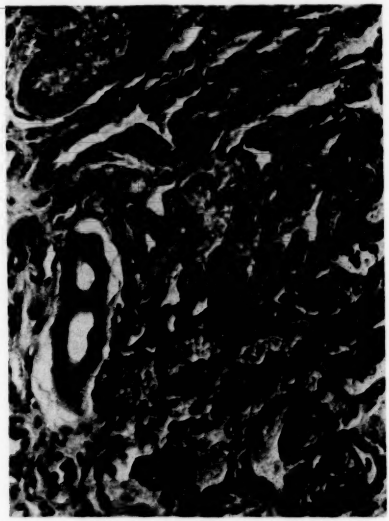

FIGURE 1. *Section of the Hemangioma of the Parotid Gland in Case 1 (Approximately X440).*
Note the parotid ductule at the lower left isolated among vascular channels composing the tumor. A small muscular artery appears at the upper left.

Interestingly enough, 36 of the 51 patients whose sex is recorded were girls.[2-6] The right and left parotid glands appear to have been involved with approximately equal frequency.[2-6] McFarland[3] recorded only 3 cases in which another major salivary gland, the submandibular, was affected.

Strikingly, 90 per cent of parotid tumors recorded in infants in their first year were hemangiomas; 88.5 per cent of recorded hemangiomas of the parotid gland affected infants of this age group.[2-6] (Tables 2 and 3). The study of Howard et al.[2] includes only 4 cases of parotid lipoma in children, 2 of adenoma, 2 of cystadenoma and 2 of secondary neuroblastoma, 1 of parotid cyst and 1 of accessory lobe of the parotid gland simulating neoplasm. Where given, the ages of these patients were two years or older. Howard and his associates[2] noted the tendency to bilateral involvement with exacerbations of acute swelling that may distinguish chronic inflammatory enlargements of the parotid gland in childhood, but despite a statement that "this disease characteristically has its onset in childhood," these authors were able to cull from the literature only 2 previously reported cases of chronic parotiditis in children and to add 2 cases of their own (one occurring at five and the other at seven years of age).

TABLE 2. *Types of Parotid Neoplasms Occurring in the First Year of Life.*

NEOPLASM	NO. OF CASES	PERCENTAGE
Hemangioma	54	90.0
Mixed tumors	5	8.33
Carcinoma	1	1.66

The value of present statistics is diminished by the probably large number of unreported cases. Reference was found in the files of one pediatric hospital to 14 unpublished cases of hemangioma of the parotid gland.[7] Nevertheless, the available statistics indicate that chronic unilateral enlargement of the parotid gland in the first year of life is usually a symptom of parotid hemangioma. Obvious hemangiomatous involvement or bluish discoloration of the overlying skin[2,3,4,6] and the compressibility of some of the lesions[4,5] lend support to a preliminary statistical diagnosis of parotid hemangioma; biopsy would be necessary, however, to exclude mixed tumor and carcinoma, both of which have been found to occur in the parotid gland in this age group.[2] In any event, surgical extirpation of the entire affected gland, subtotal parotidectomy, with excision of the lesion, or biopsy followed by x-ray therapy have been favored as satisfactory definitive treatment for parotid hemangiomas.[2-6]

TABLE 3. *Age Distribution of Patients with Hemangiomas of the Parotid Gland.*

AGE	NO. OF CASES	PERCENTAGE
yr.		
0-1	54	88.5
1-12	6	9.84
Adults	1	1.64

Because of the alarming nature of the deformity produced by these lesions,[5,6] medical attendants and parents are unlikely to discourage surgical intervention.

The choice of surgical procedure is likely to be determined by the extent of the lesion. In the cases reported above subtotal parotidectomy sufficed to excise the grossly visible tumor. In the material presented by Wawro et al.[6] the tumor was confined in a number of cases to the superficial lobe of the parotid gland, but in others the retromandibular portions were involved; in 2 cases the hemangiomas extended into the neck inferior to the clavicles, and 1 of these invaded the submaxillary and pterygomaxillary spaces. These were removed nevertheless.

Preservation of the usual lobular pattern of the parotid gland may offer diagnostic difficulty when the lesion is first examined grossly by the surgeon or pathologist. In Cases 1 and 3 reported above the lesion resembled nothing quite so much as an enlarged, coarsely lobated and cyanosed parotid gland. In Case 2 a similar lesion had evidently been torn apart during removal (Fig. 2). This gross appearance is characteristic. McFarland[3] described the lesion in his case as "more like a hypertrophy . . . than a tumour," and he noted, in 3 of the cases that he reviewed, similar comparisons with hypertrophied parotid glands. The gross illustration included by Wawro et al.[6] resembles Figure 2 above, and they described similar gross appearances.

The correct diagnosis is more obvious when routinely prepared paraffin-embedded sections are examined histologically, although in quick sections the replacement of parotid acini by a less orderly and more highly cellular tissue, together with scattered or even abundant mitotic figures, may combine to suggest malignant change if the pathologist does not consider the possibility of an endothelial tumor.

The rapid enlargement of the lesions and corresponding lack of histologic differentiation with abundant mitotic activity illustrated by Wawro et al.[6] in parotid hemangiomas encountered in the first six months of life were not observed in the cases reported above. Indeed, in Case 1, the rapid enlargement of a histologically well differentiated lesion was observed during the latter six months of the first year, and in Case 2, a well differentiated parotid hemangioma without clinical evidence of rapid growth was resected at the age of three months. The correlation between the clinical behavior of the lesion, the histologic findings and the age of the patient is not always so logical or so invariable as the cases of Wawro and his associates[6] suggest.

Forty-six cases were treated primarily by excisional surgery. Twenty-eight of these operations appear to have led to uncomplicated ablation of the tumor.[2-6] Nine patients suffered from facial palsy.[2-6] There were 5 postoperative recurrences[2,4,6] and 2 deaths.[3,6] All postoperative recurrences yielded to re-excision,[2,4,6] but in 2 cases re-excision led to facial palsy.[2,4] The extent of the operations is often not specified. Five of these patients were followed for periods of ten years or more, and 4 for periods of one to five years, during which no recurrences were detected.[2,6]

In the series of Howard et al.[2] postoperative x-ray therapy was employed in 2 cases after excision of the tumor mass, in 2 cases after biopsy, and in 1 case after partial excision. In 1 of the cases in which surgical excision preceded x-ray therapy there was no recurrence after thirteen years; 1 of those in which x-ray therapy was preceded only by biopsy showed no recurrence after five years. The 3 other patients were well at the time of the report (1950), but at

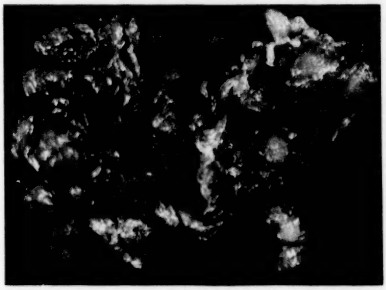

FIGURE 2. *Gross Appearance of the Resected Lesion in Case 2.*

that time only three months or less had elapsed since their treatment. No case of postoperative facial palsy occurred.

One of the cases of Wawro and his co-workers responded incompletely although favorably to x-ray therapy; in other cases the failure of x-ray and radium therapy initiated excisional surgery. Since a definitive diagnosis can be established only by biopsy, it seems only reasonable that, when technically feasible, the biopsy should be of the excisional kind. Benefits of postoperative x-ray therapy can then be weighed against the possibility of irradiation damage to the neighboring bone and eye.

Despite a note of alarm sounded by Glaser et al.[4] respecting a "uniformly disastrous course" that is "changed considerably" if surgical intervention occurs, there are but 2 references to parotid hemangiomas the courses of which, not interrupted surgically, have terminated in death with autopsy.[3] An equal number of deaths have followed operation.[3,6] Wawro and his associates[6] could find no reference to malignant variants of this lesion. Local extension beyond the parotid capsule and into the adjacent tissues should not be considered alone as sufficient evidence for a diagnosis of malignant degeneration in these tumors, particularly when viewed in the light of some of the follow-up data.

It must nevertheless be admitted that follow-up data are incomplete, and follow-up periods in some cases, of which this series is a fair example, are often very short. The prognosis for parotid hemangiomas nevertheless appears to be good. Histologic evidence of sarcoma in this lesion is lacking.[1-7] Although the age distribution is convincing evidence of a congenital origin, in none of the cases reported above were associated, clinically serious congenital lesions described, and no evidence of congenital or familial vascular dysplasias in the nature of the Hippel–Lindau syndrome or hereditary telangiectasia is known to exist in any of the families. This is in keeping with previous reports of parotid hemangiomas, and with the classic description of the Hippel–Lindau syndrome and hereditary telangectasia, in neither of which would parotid involvement be considered a typical event. In Cases 2 and 3 of this series the possibility of incomplete removal may lead to local recurrences, an event to be regarded with less concern than facial palsy. In Case 1 the recovery from postoperative facial palsy was gratifying but not entirely unexpected, for exquisite care had been taken to avoid unnecessary trauma to the facial nerve, and no large nerve segments were identified in the numerous microscopical sections.

The chief danger inherent in parotid hemangiomas appears to be permanent damage to the facial nerve during surgical removal. As Howard and Wawro and their associates have pointed out, the facial nerve is encountered in the parotid region of infants at a deceptively superficial level and is therefore susceptible to unintended trauma. In the light of what is known of the behavior of congenital capillary hemangiomas of the parotid gland, the planned resection of portions of the facial nerve as part of primary excision for this lesion could be described as an unwarranted procedure, despite the excuses that have been made for it.[4]

Summary and Conclusions

Three cases of benign congenital capillary hemangioma of the parotid gland are presented, together with a brief review of the literature on this subject. Fifty-four of 61 cases occurred in the first year of life, comprising 90 per cent of 60 reported cases of various parotid tumors occurring at this age. This age distribution is of obvious importance in the differential diagnosis of parotid enlargement occurring before the age of one year.

Most of these tumors have affected girls. Evidence suggesting a large number of recognized but unreported cases of this disease is presented. Although these lesions may be one of the variable manifestations of congenital vascular dysplasias involving structures of the head and neck, they have not yet been reported in association with serious intracranial vascular anomalies.

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OSTEOARTHRITIS OF THE CERVICAL SPINE*

Stage and Treatment

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Osteoarthritis of the cervical spine, sometimes called cervical discogenic disease, is one of the most common and most troublesome affections of the older arthritic patient. It is found in at least 10 per cent of the patients suffering from osteoarthritis. The symptoms, the clinical findings and the roentgenologic changes vary greatly from patient to patient. However, cervical osteoarthritis can be divided into three stages of progressive degeneration (Table 1). There are no diagnostic or therapeutic criteria for osteoarthritis such as those available in rheumatoid arthritis, but degrees of severity can be recognized.[1]

Stages

The first and commonest of these stages is the early stage (Fig. 1*A*). Here, there are mild roentgenologic changes, with pain, stiffness and muscular spasm in the antigravity muscles of the neck. The diagnosis of a muscular sprain of the neck is commonly made. The second or moderately advanced stage shows extensive changes in the x-ray picture, with degeneration and narrowing of the intervertebral disks (Fig.

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1*B*). The chief symptoms of this stage are neurologic. Muscular spasm and stiffness may be present but are overshadowed by the pain referred to the dermatomes of the nerve roots that are irritated. The third, or late, stage is associated with severe irreversible changes in the cervical vertebras and in their intervertebral disks (Fig. 1*C*). There are usually both severe mechanical and neurologic symptoms, with limitation of motion and with deformity in the cervical region.

Osteoarthritis may appear in early middle age and progress to the most severe stage in a few years. Fortunately, in most cases it progresses slowly. What makes for rapid progression or for a remission in symptoms is not fully understood, but mechanical stresses and endocrine disturbances seem to be important factors. The pathologic process itself appears to be a degenerative one associated with aging.

The mechanical basis for most of the symptoms that are present is more easily understood.[2] The muscular spasm and the feeling of stiffness are usually the result of sprain and overstretching of the muscles and ligaments that span the bony proliferation about the vertebral margins. The radiating pain and the other neurologic symptoms are usually the result of irritation of the nerve roots, the cervical cord or the sympathetic nerves. This irritation most often occurs at the neural foramens.[3] Most constantly found is a narrowing of the neural foramens, with impingement and irritation of the nerve roots. Although degeneration and sometimes complete disappearance of the intervertebral disks in the lower cervical region are often observed in osteoarthritis, symptoms referable to the disks are rare.[4] Myelograms have been carried out in many of these patients with osteoarthritis, and evidence of displacement of the disk has been found only rarely. It is not commonly an important factor in producing the neurologic symptoms. Degeneration of the disks, however, adds to the functional disturbance and to the deformities.[5]

TABLE 1. *Stages of Cervical Osteoarthritis.*

STAGE	VERTEBRAS	OSSEOUS SPURS	NEURAL FORAMENS	INTERVERTEBRAL DISK	MUSCULAR SPASM	CERVICAL CURVE	NERVE-ROOT PAIN
Early	Normal	Moderate	Normal	Little change	Moderate	Normal or increased	Rare
Moderately advanced	Deformity	Advanced	Narrowed	Narrowed	Severe	Decreased or absent	Present
Late	Deformity & osteoporosis	Severe	Narrowed	Absent Schmorl nodule	Severe	Decreased or absent	Present

A B C

FIGURE 1. *Stages of Osteoarthritis of the Cervical Spine.*
A = *early stage, showing slight bony proliferation, with little change in the intervertebral disks.*
B = *moderately advanced stage. There is extensive bony proliferation about the vertebral margins. The intervertebral disks are narrowed, particularly in the lower cervical region.*
C = *late stage. The normal cervical lordosis is lost. There is extensive bony proliferation, with vertebral deformity. The intervertebral disks are all narrowed, with disappearance of the disks in the lower cervical region.*

TREATMENT

Treatment in the early stage is directed to relief of the sprain and to improvement of the medical and mechanical faults that are present. Soreness and spasm are usually treated most effectively by temporary support. A padded collar, which fits the con-

tours of the shoulder and jaw, should be worn until symptoms subside. The collar is removed several times a day for the application of heat to the back of the neck. To lessen the tendency to sprain, the posture of the patient should be improved. The patient should sleep on a firm bed with only one small pillow, which can be fitted into the nape of the neck for greater comfort. Sitting should be in straight-backed chairs, which support the entire spine. Obesity and dietary faults should be corrected. Obvious endocrine

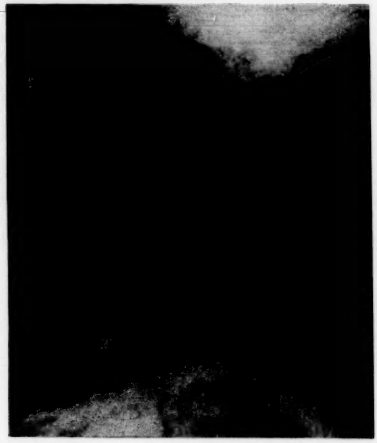

FIGURE 2. *Late Stage of Cervical Osteoarthritis, with Extreme Bony Proliferation about the Vertebral Bodies. The vertebral disks are narrowed. The intervertebral joints are narrow, but there is no ankylosis.*

disturbances should be treated. Symptomatic foci of infection should be corrected or removed. It is not known that they have any direct influence on the osteoarthritis, but many patients have experienced prolonged improvement of symptoms after the removal of such infections. In this early stage symptoms are usually relieved readily by improved alignment of the neck, temporary support and mild physiotherapy. Medicines, beyond mild sedation, are rarely required.

In the moderately advanced stage, although muscular spasm and sprain may be found, the symptoms are usually neurologic. These symptoms are chiefly radiating pains, which may be constant but which are aggravated by activity. There are 8 pairs of cervical nerves emerging from the neural foramens and 3 pairs of sympathetic ganglions with communications with the cranial nerves. It is not surprising that varied and unusual neurologic patterns arise.[6] In addition pressure can occur upon the cervical cord from the bony proliferation and occasionally from the displacement of a degenerated intervertebral disk or a cervical vertebra. When symptoms are severe the normal cervical lordosis may be lost.[7]

Treatment is aimed at relieving the pressure on the nerves, by restoration of a more nearly normal angulation and alignment of the neck. Such a realignment increases the diameter of the neural foramens. Usually, the symptoms are relieved quickly; the cranial nerves can undergo considerable irritation without permanent damage. A firm bed with no pillow or only a small one under the nape of the neck is advised. Support and heat are used. In most cases relief follows the almost continuous application of traction of 5 to 10 pounds to the cervical spine with the patient supine on a firm bed. When there is extensive osteoporosis or severe vertebral deformation, heavier traction with tongs attached to the skull may be required. X-ray treatment[8] or ultrasonics[9] have been found helpful occasionally.

If no improvement in nerve-root pain follows the use of traction for two weeks, the pressure on the nerve must usually be relieved surgically. Lumbar puncture and a cervical myelogram are then carried out to determine where there is pressure. It is better to withhold cortisone and its analogues in this stage since they mask symptoms and often delay proper diagnosis and treatment. The pressure is usually found at one or more neural foramens. Treatment consists in the surgical relief of this pressure by removal of the posterior portion of the intervertebral joint or by enlargement of the neural foramens. Surgery is rarely required for the removal of disk substance. Usually, a support must be worn, and physiotherapy must be given for a number of months after surgery.

In the late stage there are symptoms both from mechanical derangement and from nerve irritation. The changes in the spine and its contiguous tissues are for the most part irreversible.[10] For this reason treatment and support must usually be continued throughout the patient's life.

Treatment in this late stage is wholly symptomatic. Traction may give temporary relief. The most effective treatment is a firm, snugly fitting collar. This should be made from a plaster model that fits over the shoulders and gives support under the occiput and the chin. This can then be molded in leather or in plastics and can be fitted with straps to facilitate removal for bathing of the skin. X-ray treatment and surgery are rarely indicated in this final stage. The completely degenerated disks practically never give symptoms of pressure.[11] Occasionally, Schmorl's nodules can be seen in the vertebral body, but usually the disks simply disappear.

END STAGES

Three end-stage conditions are found with osteoarthritis in the cervical spine. The most common is extreme bony proliferation about the anterior mar-

gins of the cervical vertebras, leading to very limited motion or loss of motion in that portion of the spine[12] (Fig. 2). The next most common is a gradual forward subluxation of a cervical vertebra, usually the fourth or fifth (Fig. 3). This is never great in extent and rarely leads to exacerbation in symptoms.[13] The least common of the end stages is that associated with osteoporosis, in which there is a shortening and forward displacement of the cervical spine. Osteoporosis, with collapse and displacement of cervical vertebras, is always associated with severe neurologic symptoms (Fig. 4).

Discussion

When more is known about the various factors that bring on the rapid changes in osteoarthritis more will be possible in prevention. At present all one can suggest when symptoms of osteoarthritis appear in the cervical spine is less strenuous work, more rest, support to the cervical spine, improvement in posture, a high-protein, low-carbohydrate diet, correction of endocrine disturbances and elimination of known infection. Although cortisone and its analogues[14] and phenylbutazone lessen pain in many cases, they have no known effect on the degenerative process itself. One is left with symptomatic relief of symptoms as they arise and a reasonable regulation of activity. Surgery (occasionally) and constant firm support to the neck are helpful. Although most patients improve greatly with symptomatic treatment, recurrences in symptoms are common unless the patients are kept under constant medical supervision.

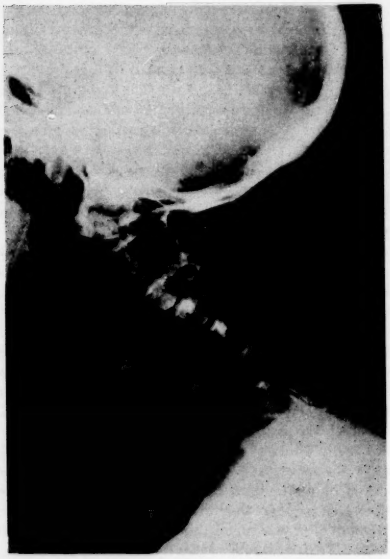

Figure 3. *Late Stage of Cervical Osteoarthritis, with Subluxation of the Third Cervical Vertebra on the Fourth and the Fourth on the Fifth.*
The normal cervical lordosis is lost. The intervertebral disks are almost gone in the lower cervical region. Several Schmorl nodules can be seen.

Figure 4. *Late Stage of Osteoarthritis of the Cervical Spine. All the vertebras show osteoporosis. The second cervical vertebra has collapsed. (Only osteoporosis was found at autopsy.) There is extreme osseous proliferation and vertebral deformity.*

Summary and Conclusions

Symptomatic osteoarthritis of the cervical spine is found in about 10 per cent of the patients seen in the arthritis clinic. Usually, the disease shows gradual progression in pathologic changes and in symptoms. Three progressive stages can be recognized. In the early stage one finds the symptoms of sprain in the cervical spine. Treatment is chiefly support and physiotherapy. In the moderately advanced stage symptoms are mainly neurologic. These symptoms are relieved by cervical traction and by support of the neck. In the more severe cases, surgery to relieve pressure on the nerve may be required. Evidence of

pressure from degeneration of cervical intervertebral disks is not often demonstrated. In the late stage irreversible changes are often found in the cervical spine. Symptoms are both mechanical and neurologic. Treatment is symptomatic, varying with the severity of the disease. In most cases pain and disability can be relieved. Medical supervision should continue for the remainder of the patient's life.

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MEDICAL PROGRESS

TREATMENT OF LEPROSY

II. The Role of Surgery

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BEFORE the present decade, surgery on the patient with leprosy was mainly a retreating battle against advancing deformity. When ulceration of fingers or toes deepened to cause osteomyelitis, necrotic bone was removed. When ulceration became too widespread on the front of the foot, a partial amputation was performed. Higher amputations followed when the stumps themselves became destroyed. A few surgeons had attempted reconstructive surgery to the extent of excising nodules from ears and unsightly loose folds of skin from the face in arrested cases, to make it easier for the patients to rejoin society. Leprosy was regarded by most as a grossly destructive disease and any more extensive constructive or reconstructive surgery as doomed to failure.

The present marked change in attitude has been due, in part at least, to the more hopeful outlook as far as arrest of the disease is concerned. The sulfones have made more probable a return to a noninfectious state for the patient, and it is clearly important to do everything possible to prevent or overcome deformities that would otherwise remain as severe handicaps.

The second major factor that has encouraged reconstructive surgery is a change of emphasis in understanding of the cause of deformity in leprosy.

To the layman, and perhaps to most physicians also, the best known feature of leprosy is the gross deformity that results from loss of digits or more extensive destruction of the extremities. Most people who have worked with patients with leprosy have realized that a certain proportion of this loss of tissue has been due to direct injury and secondary sepsis, associated with loss of pain sensation. A large part of the damage, however, has been thought to be caused by an absorptive process regarded as an integral part of the disease.

Dr. Robert Cochrane, a noted specialist in leprosy, once referred a patient with leprosy to me (I was then a young surgical colleague) for partial amputation of a badly absorbed and ulcerated foot. He remarked that the tissues of leprosy healed better, in his experience, than normal tissues. This rather unlikely statement was too much for me to accept, but it started an investigation of wound healing, and of the natural history of absorption and deformity in leprosy, that later led to a program of reconstructive surgery. It seemed unlikely that a process that was causing active absorption and destruction of tissue could allow normal or better than normal wound healing in the same area: either the disease was not really tissue destructive, or wound healing would not prove to be normal. The two problems should be studied together.

Tissue Absorption

A close analysis of a number of the histories of deformed patients shows some interesting features. One is that the absorption of hands and feet occurs earlier and more seriously in the tuberculoid type of leprosy, in which the bacilli are less evident and in which they are usually absent from bones and deeper structures. When absorption of digits develops in lepromatous patients it is often later in the disease, when there are few bacilli, or even after the patient has become bacteriologically negative on routine smears.

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Many patients can remember incidents of trauma or burns, with sepsis, in association with most of the episodes of shortening of fingers. Even in well organized leprosariums it is common to find untreated and unnoticed open wounds on many anesthetic hands. In 1 leprosarium of less than 200 patients, over 90 such open cuts and burns were found at a single inspection. None were causing any concern to the patient, and they had not been thought worth reporting to the physician.

If mere anesthesia of the hands allows such frequent and continued secondary sepsis, it scarcely seems necessary to invoke a specific destructive process in leprosy. Preliminary surveys suggested, more than five years ago, that injury and sepsis and trophic change were responsible for by far the greater part of so-called leprous tissue absorption. It is difficult, however, to define with precision the role of leprosy per se in absorption of digits, because in many wounds at least two pathologic processes may be simultaneously at work: the leprous process and the simple traumatic and septic process. The practical significance of the distinction is that if anesthesia and carelessness are responsible for finger absorption, it should be possible to show that absorption is preventable, even when the disease is not cured.

A rehabilitation center for deformed patients with leprosy has been observed from this point of view. For the past five years it has contained 15 to 20 men, all of whom have anesthetic hands, and many of whom have partial loss of some fingers. Every patient does six hours of manual work each day, usually carpentry.

Great attention is given to hands. Frequent inspection emphasizes the gravity with which even the smallest cut or abrasion is regarded. Work and leisure are studied so that possible sources of injury may be avoided.

During these five years only 2 fingers have become shorter after admission to the center. In each case the shortening followed osteomyelitis of the terminal phalanx and sequestration of its tip; the losses in length were 0.6 cm. and 0.8 cm. In 1 case a known injury precipitated the infection; in the other no history of injury was remembered, but the infection was observed to follow the typical acute course of a whitlow or felon, with local redness and swelling, fever and lymphadenitis, thick pus being found in the pulp on incision. The bone was bare in the abscess when it was opened, and later its tip sequestrated and the wound healed rapidly, leaving the shortened finger and scarred pulp.

Apart from these known secondary infections, all fingers have maintained their length. It is true that the study covers only about 90 patient years, but patients were selected because they were high-risk types, with very many digits in process of absorption. This five-year halt in almost every absorptive process, therefore, is thought to have some significance.

Although it is not yet possible to define exactly the role of leprosy in tissue absorption, it seems justifiable to conclude that if anesthetic hands can be guarded with more than ordinary forethought and care, they will not usually become absorbed. There is no doubt that anesthetic hands of patients with leprosy are not as well able to bear stresses and strains as normal hands. This is common to any limb denervated from any cause.

In my opinion one reason that leprosy has gained its reputation as a destructive disease is that anesthesia to pain occurs far in advance of muscular weakness. When there is loss of pain from other causes there is often also total paralysis of the limb, and therefore less hazard of injury. In the few cases of leprosy with really severe and early muscular paralysis that I have seen, there has been no absorption at all.

Wound Healing

No properly controlled experimental study of wound healing in leprosy has yet been carried out. In this clinic, however, over 800 operations on the hands and feet of patients with leprosy have been performed, and the healing process has been followed with some care and attention. In the same clinic many orthopedic and plastic reconstructions have been carried out on the hands of nonleprous patients.

It has been my impression that although most wounds in leprosy patients heal normally, delay in union may result from a poor nutritional state, which is common in these patients. Also, anesthesia of the wound area deprives the patient of normal protection. It is good practice, therefore, to leave the skin sutures in place for two or three extra days. Gross sepsis has occurred in only 1 case although stitch abscesses and other superficial infection have been about as common as in the hands of nonleprous patients.

Skin flaps and tubes have been transferred, the same rules as apply to healthy persons being used, and with at least as good results. Free grafts have taken with more regular success than in other cases. Tendon suture and free tendon grafting have been performed in hundreds of cases and with more regular success than in any similar series that I have seen of traumatic or other injuries. This success is probably due in part to the fact that postoperative exercises are not inhibited by pain.

Motor Paralysis

When it had been established that wound healing offered no special problem and that tissue absorption need not destroy reconstructed hands, it remained to find out whether the paralysis of leprosy was of a type to encourage attempts at restoration of muscle balance.

As early as 1890, Gerlach, Dehio, Woit and others had noticed that motor nerves were paralyzed according to a more or less regular pattern in leprosy. The pathologic significance of this observation has given rise to speculation, but its significance to surgeons has escaped notice.

Paralysis surveys at Vellore represent an examination and assessment of several hundred patients who have presented themselves at the hand clinic for treatment of deformed or paralyzed hands. These have been supplemented by the examination of about 2000 hands at leprosariums, assessed by the same team.

The hands fall into three well-defined groups:

Group 1. Forty-six per cent of all the hands presented for surgery at the hand clinic had a pure ulnar palsy, with no other motor-nerve damage. This percentage was higher in the wider surveys, where mild and early cases were included.

These patients may have anything from minimal small-muscle weakness up to total paralysis of all ulnar-supplied muscles in the forearm and hand. The disability may be a clawing of 2, 3 or 4 fingers, and there may be some instability of the thumb in pinching.

Group 2. Fifty-two per cent of the patients seen in the clinic had a total paralysis of all the ulnar-supplied muscles, in addition to a paralysis of the median-supplied muscles below the wrist. This group had clawing of all fingers, and a thumb that was unable to abduct or oppose the fingers in grasp or pinch.

Group 3. One and five-tenths per cent had a total ulnar paralysis, a median paralysis below the wrist and a total paralysis of radial-supplied forearm muscles.

This group had the same disabilities as Group 2, with the addition of wrist drop and a paralysis of all finger and thumb extensors. These are indeed totally useless hands.

The remaining 0.5 per cent consisted of unusual tuberculoid and dimorphous cases with pure median paralysis or high median paralysis. These cases are quite exceptional.

The striking feature of the pattern of the motor-nerve involvement is that leprosy seems to paralyze one main nerve at a time. It attacks nerves in the same order, at exactly the same level in every case, and it paralyzes no muscles above the elbow.

From a practical point of view, the most useful finding from these surveys is that the median nerve above the wrist is spared in leprosy.

Even in the absolutely helpless hand of Group 3, with complete clawing and extensor palsy, there are at least 10 useful and powerful forearm muscles remaining. They are all flexors, and are useless only because they are unbalanced by extensors and stabilizers. A five-year follow-up study on many of the earlier hand-reconstruction operations has shown that these median-supplied forearm muscles continue to function and even to improve their range and power after transfer of their tendons to restore muscle balance to the hand.

Hand Surgery

If the limitation of the destructive and paralytic processes in leprosy is accepted, the treatment of deformity becomes a matter of applying well established physical and surgical methods in a new field.

For the ulnar paralysis a muscle-balance operation is performed to restore the lumbrical component of finger movement. In most of these cases the Bunnell sublimis transplantation is used. For ulnar and median paralysis, this operation is extended to all fingers, and supplemented by an opponens and abductor transplant for the thumb. If there is also radial palsy a wrist arthrodesis is first performed, and then the median-supplied wrist flexors and the pronator teres are transferred around the forearm to act as finger and thumb extensors.

Physiotherapy

The most essential part of any hand-reconstruction center is a well staffed physiotherapy department. The work of the Department of Physical Therapy at Carville, which was greatly extended in 1947, has been ably described by Hatch. On the whole, the results have been good, both physically and psychologically.

In a hand that has remained mobile in spite of paralysis, transplantation of tendons does not offer many unusual problems. Unfortunately, however, in many cases that come for surgery there is joint stiffness and scarring. Disuse and misuse have left a distorted and stiff hand, often with neglected ulcers.

In earlier attempts at reconstruction, many of these hands were classed as hopeless. Arthrodesis of interphalangeal joints in the position of function seemed to offer, at best, promise of only a moderately useful hand. Experience, however, has shown that the prognosis for mobility is very much better than was anticipated. The anesthesia that contributed to the deformity, and may have been the primary cause, allows the hand to recover far better than its more sensitive fellow.

Daily treatment with exercises and wax baths, with corrective splintage between exercises, will restore many a rigid finger to mobility. Even when the joint has been damaged by sepsis, the cartilage is eroded and the capsule is contracted, useful movement is often possible. It is true that there may be crepitus as the joint moves, and that such movement would be impossibly painful if sensation were to be restored, but these things do not worry the patient. He is safe in his anesthesia, and his hand has become useful again. This may be called a Charcot joint, but to him it is a functioning finger.

At various stages in the mobilizing process the surgeon must be prepared to intervene by inserting a free graft of full-thickness skin when skin is limiting mobility. This is most commonly required on the back of the hand to allow the thumb to be abducted and rotated forward. Finally, when the joints are fully mobile, the surgeon assesses the paralysis and operates to restore muscle balance.

It is now quite exceptional to find a hand so far damaged by leprosy that it is not possible to restore

to the patient at least the power to grasp strongly with his fingers and hand, and to pinch firmly between thumb and fingers. These movements may allow him to feed and dress himself, and even to meet most of the requirements of certain manual trades.

Denervated Feet

In the foot a similar pattern and limitation of paralysis has been found. The plantar-flexing and inverting muscles are unparalyzed, whereas the dorsiflexing and everting muscles, and all the small muscles, may be paralyzed. This leads to clawing of the toes and to foot drop. Both these disabilities are correctable. I have been using a transfer of the tibialis posterior to the dorsum of the foot to correct foot drop, and a dorsal transfer of digital flexors for claw toes.

These corrections may improve the gait, but they do not solve the greatest problem in the feet — that of trophic ulceration. There does not seem to be any ready solution to this problem. The patient should wear shoes that distribute the stress of weight bearing evenly over the sole of the foot and should refrain from standing for prolonged periods, and from long walks. In other words, he should learn the limitation of his feet.

Facial Deformity

One of the greatest handicaps of the patient with healed leprosy is sometimes the appearance of his face. He may no longer be infectious but may carry disfigurements that separate him from his fellows more effectively than segregation laws. Many of the classic deformities have proved amenable to plastic surgery. The transfer of hair-bearing skin to the eyebrows, the building up of the depressed nose with cartilaginous, bone or acrylic implants, the removal of unsightly excessive skin folds and the performance of tarsorrhaphy to correct lagophthalmos will do more than improve the appearance of the patient's face: these operations may restore courage and faith to a man who had lost all hope of being able to begin a new life.

This is the time for the orthopedic and plastic surgeon to come forward and open the door that leads the leprosy patient from isolation back to his family life and job.

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MEDICAL INTELLIGENCE

SALPINGITIS DUE TO *ENTEROBIUS VERMICULARIS* *

Report of a Case

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Enterobius (formerly called *"Oxyuris"*) *vermicularis* is the most common metazoan parasite of man. Despite its world-wide prevalence, its pathogenicity is very low, and it rarely strays from its usual habitat in the intestinal tract and the perianal skin. It is our purpose to report the case of a girl in whom the organism apparently caused a salpingo-oöphoritis, and to review briefly the literature of atypical infestation.

The infestation, though extremely prevalent, is quite variable throughout the world, in various sections of the country, and even in various social classes. Thus, Weller and Sorenson[1] reported a prevalence of 19 per cent in 565 children at the Children's Hospital in Boston, and Cram[2] 41.5 per cent in 2895 white people and 12.9 per cent in 1097 Negroes in Washington, D. C. Because of low pathogenicity, the vast majority of cases are almost entirely asymptomatic; symptoms are limited usually to the pruritus caused by the nocturnal perianal migration of the worms.

That parenteral infestation by *E. vermicularis* does rarely occur is well documented by several authors.[3-5] How and why it occurs is not well understood.

Enteric infestation is established in one of four ways[6,7]: Type D (digital infestation), the commonest type, is established by transfer of ova from a patient's

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perianal skin to his mouth or nose on his fingers; Type C (contact infestation) results from intake of food contaminated by fingers, flies or dust; Type S (Straub infestation) results from contaminated dust; and Type R (retrofection) is due to larvae, which hatch in the anal region and pass back into the anus to mature (the female is fertilized and passed out again to the perianal skin to oviposit, thus renewing the cycle of infestation).

It is obvious that none of these methods of infestation explain the occasional parenteral infestation. As a possible explanation of this phenomenon, a new pathway, the "urogenital migration," has been postulated. In Scotch-tape preparations of the perianal skin Beaver[8] has found mature females, immature females and even males. Ordinarily, the gravid female worm migrates to the perianal skin, there to oviposit for the continuation of the species. Under extraordinary circumstances the worm fails to oviposit on the skin but elects instead to re-enter the body via the urogenital tract, usually migrating through the female genital tract and even reaching the peritoneal cavity, ovipositing en route. It has been suggested[3] that the urogenital migration might be a chance migration into an adjacent orifice, the worms reaching the perianal skin prematurely owing to changes in the rectocolic environment from unassociated diseases.

Symmers,[4] in an exhaustive review of the pathology of *E. vermicularis* in atypical locations, found lesions containing worms or ova recorded in the literature as follows: in the cervix in 1, in the fallopian tubes in 4 and in the pelvic peritoneum in 18 cases. An analysis of the case histories revealed that infestation of the lower genital tract was usually manifested by mucopurulent, occasionally blood-tinged discharge whereas the infestation on the upper genital tract, including the fallopian tubes and adjacent peritoneal surfaces, was often characterized by only transient symptoms and signs and therefore usually discovered coincidental to surgery for some other cause. Symmers added 3 cases of his own — 2 of the pelvic viscera and 1 of the upper genitourinary tract. More recently Fatheree et al.[3] reported a case in a twenty-six-year-old woman with parasitic invasion of the uterus; the uterus was removed because of severe dysmenorrhea and the finding of a nodule in the posterior uterine wall at laparotomy. Gill and Smith,[5] even more recently, reported 2 cases of involvement of the ovary, 1 case containing ova, and the other containing ova and degenerated worms. Both these cases were incidental findings during pelvic surgery for other causes and did not produce any symptoms in the opinion of the authors.

There is little doubt that the female genital tract serves as the chief, if not the only, route of invasion to explain these peritoneal lesions. These lesions have not been observed in the male; various stages of infestation of the female genital tract have been authentically observed, and finally the peritoneal lesions are most commonly observed in the pelvic cavity in close proximity to the upper genital tract.

The gross and microscopical description of the lesions found in the peritoneal cavity follows a characteristic pattern according to the age of the lesion. The older, well encapsulated lesion is described by Symmers[4] as being 1 cm. or less in its greatest dimension, firm and white, with a yellowish center. Microscopically, the lesion consists of a capsule of fibrous tissue, infiltrated by groups or even follicles of lymphocytes. Internal to this is usually a zone of granulation tissue surrounding a core of necrotic substance consisting of the parasite, or its remains, and ova. In the older lesion only the ova may remain, since they are more resistant than the parasite. Eosinophilic granulocytes, foreign-body giant cells and Charcot–Leyden crystals may be found in the earlier lesions.

Case Report

M.M., a 15-year-old girl, was admitted to the Worcester City Hospital on the Emergency Ward on November 23, 1954, complaining of lower abdominal pain of 4 days' duration that had appeared near the close of the last menstrual period, which had begun on November 15. It was sharp, intermittent, nonradiating and as marked on the right as the left side. There was associated anorexia and nausea, but no vomiting, chills or fever. Bowel habits were regular, and there were no urinary-tract symptoms. She complained of a slight leukorrhea for the preceding 2 months. The menarche had begun 2 years before admission, with regular menses occurring every 28 days and lasting 4 or 5 days. The past history indicated that she had been raped at the age of 5. The family history was noncontributory.

Physical examination showed moderate deep tenderness in both lower quadrants, with mild rebound tenderness. No abnormal masses could be felt at this time, either abdominally or on rectoabdominal or vaginoabdominal palpation, though there was considerable tenderness on motion of the cervix.

The temperature was normal.

Several white-cell counts varied between 6000 and 9000, with 3 or 4 per cent eosinophils. The erythrocyte sedimentation rate was 21 mm. per hour.

The patient improved with bed rest, and was discharged on the following day, only to return the same evening complaining of gradually increasing pain in the left lower quadrant of the abdomen. On rectal and vaginal examination during the next few days, a persistent tender mass was palpable in the region of the left adnexa.

At operation on December 2, through a Pfannenstiel incision, a left salpingo-oöphoritis was found, involving the distal third of the tube and the ovary in a contiguous acute inflammatory mass. The 2 were readily separated, and a thick layer of fibrin separating them was removed for culture, direct smears and microscopical examination. Both ovary and tube were intact, and no pus or fluid could be expressed from the tube. At this stage the surgeon thought that the lesion was bacterial in origin and could be handled with antibiotics. A prophylactic appendectomy was done.

The smears, however, revealed no organism, and the cultures produced no growth. Furthermore, the microscopical report indicated "fibrin-containing polymorphonuclear leukocytes, plasma cells, macrophages and ova and fragments of unidentified parasite, probably *E. vermicularis*." The appendix contained no worms. Slides were subsequently submitted to the Armed Forces Institute of Pathology, whose staff considered the ova consistent with *E. vermicularis*. The microscopical appearance of the specimen is shown in Figure 1.

After the pathological report was received the stools were examined, and ova were seen that were consistent with *E. vermicularis*. On requestioning the patient stated that for 1 month before admission she had noted a moderate pruritus ani and vulvae, but at no time had she noted any worms. There was no family history of infestation. The patient was discharged on December 10 after an uneventful convalescence. Follow-up study has revealed occasional pain in the left lower abdomen, which is worse during menstruation.

Summary and Conclusions

The parenteral infestation of *Enterobius vermicularis* is briefly reviewed.

The rare "urogenital migration" of the gravid worm through the female genital tract to oviposit within the peritoneal cavity seems to be the most plausible explanation for the lesions described in the literature.

A case that was unusual in that the symptoms and signs developed under hospital observation is reported. The symptoms and signs seemed to be directly related to local host reaction to invasion of the parasite, and the microscopical appearance was consistent with the clinical stage of the lesion.

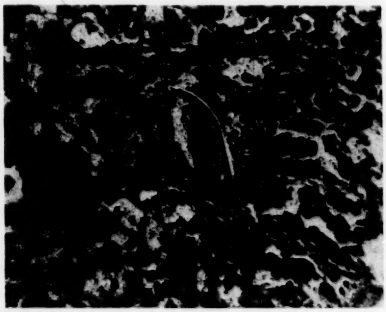

FIGURE 1. *Granulation Tissue from the Surface of the Left Tube and Ovary, Showing the Ovum of* Enterobius vermicularis.

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ON CONCEALING DEATH FROM THE PATIENT

WALTER J. FREEMAN, M.D.*

BALTIMORE

In calm I watch her die, see the last
Irregular sighs, observe the spreading stains
Of stagnant blood suffuse the lower thigh,
And prove in her eye by collapsed retinal veins
Cessation of an inaudible heart.
Outside the children cluster. Middle-aged
And worldly-wise, they know their proper part,
Cannot be overwhelmed by death engaged
For twenty years. This is the last decay.
She dies so well, dwindling unaware
To coma as to sleep with little play
Of words. She's little left with which to care.
I hear laments but no disturbing cries;
This is the way a civilized person dies.

The moving ribs, the glittering eyes — no more.
Thus Roland died, sounding a final blast
That called an army back to Christian war,
Telling God and earth that here he passed
His life. Death was there in medieval clothes,
The cloak, Mantegna's bones and Bosch's nose,
The essential serf carrying blood and ash,
Gleaning in fever, hemorrhage and rash,
Ignored while courts of vast concern arose.
Saints and prophets gladly held debate,
And angels spoke with sentient men in throes
Of mortal loss and fear inconsolate.
By hope and pained awareness sorely tried,
This was the way an early Christian died.

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CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 42021

PRESENTATION OF CASE

A twelve-year-old girl was admitted to the hospital because of swelling of the right mandible.

Progressive enlargement of the right mandible, beginning eighteen months previously, had been noted. At that time the right first and second mandibular molar teeth were extracted at another hospital. Biopsy of the mandible was said to have shown chronic osteomyelitis. An impacted right third mandibular molar tooth was removed fourteen months before admission, and two months later a bite plate was made to relieve pressure on the right mandible by the maxillary teeth. Serum calcium, phosphorus and alkaline phosphatase were normal. Because of impingement upon the mandibular mass the right first and second maxillary molar teeth were extracted five months before admission. Bleeding associated with these extractions was said to have been excessive. A marked increase in size of the mass was noted during the four months before admission.

Dental care had been good in the past. There was a questionable thrush infection of the mouth at the age of one month. A tonsillectomy for tonsillitis had been performed at the age of two years. A postnasal drip was treated with superficial x-ray therapy when the patient was four and a half years old. Two years before admission enlarged nonsuppurative lymph nodes were noted in both axillas. Earaches in both ears had occurred once or twice during the preceding year.

Physical examination showed a well nourished girl with facial asymmetry caused by a large right mandibular mass. There was no lymphadenopathy. Prominent veins were noted in the skin overlying the mass. Oral examination revealed a hard, nontender right mandibular mass measuring 8 to 10 cm. in largest diameter. It extended from distal to the second premolar tooth slightly below the mylohyoid ridge upward along the ascending ramus. The gingiva overlying the mass was not ulcerated and appeared whitish pink. Elsewhere the gingiva was normal. There was good dental hygiene, and the teeth were in good repair. No developmental abnormalities were noted. The first and second right maxillary and first, second and third right mandibular molar teeth had been removed.

The temperature was 99.7°F., the pulse 106, and the respirations 20. The blood pressure was 110 systolic, 80 diastolic.

Urinalysis was negative. Examination of the blood revealed a hemoglobin of 14.4 gm. per 100 ml. and a white-cell count of 9000. X-ray films (Fig. 1) showed

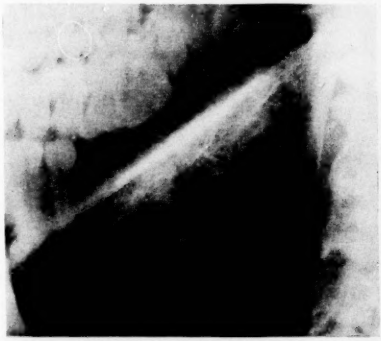

FIGURE 1. *Lateral View of the Right Mandible, Showing Marked Expansion of the Bone, Thinning of the Cortexes and an Irregular, Fine, Lacy Osseous Network through the Expanded Area.*

a diffuse, progressively expanding lesion involving the ascending and horizontal ramus of the right mandible to the region of the second bicuspid tooth. The bone appeared rarefied and contained irregular bony septa traversing it. The cortexes were thinned. All the right mandibular molar teeth were absent except for an unerupted impacted molar, which lodged in the ascending ramus and extended into the coronoid process. This tooth was subsequently removed.

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. KURT H. THOMA*: I am not clear about whether the mass described was a soft-tissue mass peripheral to the bone or whether the entire swelling was an expansion of the bone itself. From the x-ray films I am inclined to believe that there was expansion of the mandible and not a peripheral tumor mass.

DR. DAVID WEISBERGER: That is correct; the cortex of the bone was intact.

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DR. THOMA: The x-ray films show that the tumor has greatly expanded the bone; the cortex is very thin, but it is not broken through (Fig. 1). In other words the lesion was confined within the cortexes. There is no evidence of periosteal apposition at the periphery of the bone. The spongiosa itself shows an interesting alteration, however; it is quite atypical. I have seen only one similar x-ray picture of the mandible, and that was of a patient with an angioma of the jaw. Long bone trabeculae, which give the x-ray films this unusual pattern, are evidence that osteogenesis as well as resorption of bone has taken place.

The first question I have to answer is whether this mass is malignant or benign. As in all these clinicopathological cases there are several "red herrings" that are likely to mislead one. According to the history there was lymphadenopathy. If the patient had a lymphadenopathy that was not inflammatory, she may have had a lymphoblastic disease such as lymphosarcoma, but since no lymphadenopathy, either regional or generalized, was mentioned on physical examination, perhaps I can rule this out.

Next, I have to take into consideration the two biopsies. The biopsies probably were taken in the site of the tooth extraction, and since the x-ray film shows the involvement of this part, it may be assumed that they were taken from the lesion. At biopsy there was considerable bleeding. The excessive bleeding would, of course, be expected with angioma. As a matter of fact there are cases on record in which biopsies of angiomas of mandibles have resulted in death; in others the hemorrhage has been arrested only by blocking the wound with the finger or thumb of the gloved hand until a ligation of the external carotid artery could be performed.

The malignant tumors of the jaw that occur in children are undifferentiated epithelial tumors, lymphosarcoma, osteogenic sarcoma and Ewing's tumor. Lymphosarcoma, which does not as a rule expand the bone, produces osteolytic defects without bone reaction, so that I think I can rule out lymphosarcoma. Osteogenic sarcoma is a consideration since the skin over the swelling was said to have shown outlines of blood vessels. This appearance is common in osteogenic sarcoma. It is likely to produce bone and cartilage as well as soft tumor tissue. The last causes osteolytic changes. The patient had a long history, however, so that if the lesion was an osteogenic sarcoma it was not very malignant.

Ewing's tumor of the jaw is rare; I have seen only 2 patients in the second decade of life with that tumor. Although the biopsy reported to show osteomyelitis may be another "red herring," one should remember that Ewing's tumor is frequently mistaken for osteomyelitis. I do not know whether or not the biopsy was done here. A pathologist who is not used to oral pathology frequently makes the mistake of diagnosing hemopoietic tissue as chronic infection. I have observed a case of plasmacytoma that involved the jaw and was mainly contained in the bone, which on biopsy was reported as chronic inflammation, mostly plasma cells. The presence of cells that look like inflammatory cells is not astonishing at this age because there is considerable red marrow in the mandible during the first and second decade from which tumor might form. Later, the red marrow is replaced by fatty marrow. Ewing's tumor is also often mistaken for osteomyelitis in the x-ray films, but I do not think one could interpret the x-ray films in the case under discussion as chronic osteomyelitis. Furthermore, Ewing's tumor is supposed to expand in both directions — that is, it produces a peripheral mass as well as a central lesion of the bone. As we have just heard, no peripheral mass was present.

Among the benign tumors, I have mentioned angioma. From the x-ray findings this is the diagnosis I should favor. X-ray films are not diagnostic, however, as far as the histology goes, and we know that one can easily make a great mistake by "sticking one's neck out" on an x-ray diagnosis. The value of the x-ray films is to show the amount of bone involved, the presence of expansion, the involvement of the cortex and anatomical relations.

The ameloblastoma one would always consider in a child because it generally has its origin from tooth development. Ameloblastomas, however, either are unilocular and look like a cyst or are multilocular and produce rounded, circular lesions, rather than the type of lesion seen in the x-ray films of our case.

A myxoma or fibromyxoma occurs in childhood and expands the bone considerably. I have seen a child within the past two years with a tumor in the symphysis of the mandible about the size of a grapefruit that had developed from a very small central lesion by expanding without perforating the bone. In myxoma there is generally no osteogenesis: there are no bony spicules. The tumor usually looks cystic or honeycombed in the x-ray films. I do not think these x-ray films show a honeycombed type of tumor.

The other diagnosis that I should favor is fibrous dysplasia or fibro-osteoma. Fibrous dysplasia is common in the jaw in the second decade of life. It causes an extensive expansion of bone and asymmetry of the face. It is progressive and frequently causes intraoral enlargements that interfere with the occlusion of the teeth as in this case. It can produce a great variety of x-ray pictures. It will produce resorptive changes due to osteoclastic activity and new formations by osteoblasts, which are not differentiated enough to produce normal bone and therefore lay down osteoid in irregular fashion that becomes more or less calcified. I have seen some cases in which there was nothing but fibrous marrow and some cases in which newly formed, irregular trabeculae of bone were present. That picture is seen frequently in chronic osteomyelitis, particularly of the type known as Garré's osteomyelitis. In the x-ray film the affected part of the

mandible sometimes looks like ground glass, with destruction of the entire architecture of the bone and replacement by tissue that is almost uniformly radiopaque. Of course, expansion of the bone is always present; the cortex may be thinned out but is not broken through. In the x-ray film the part involved by fibrous dysplasia is not well demarcated. There is no cystic outline. Generally, it is difficult to tell how far the disease extends. In time a great deal of bone is laid down, which then becomes visible in the x-ray films. Some of the lesions in the x-ray films are described as honeycombed, others as looking like an orange peel, and still others as being trabeculated.

I believe that only the pathologist can make a diagnosis in such a case; therefore, I hesitate to give a diagnosis on the basis of what I know so far.

DR. BENJAMIN CASTLEMAN: As I understand it, Dr. Thoma, you suggested fibrous dysplasia and angioma: angioma from the x-ray films and fibrous dysplasia from the clinical picture.

DR. THOMA: Yes.

DR. CASTLEMAN: This patient was sent to Dr. Weisberger about a year before admission. Have you a comment, Dr. Weisberger?

DR. WEISBERGER: When I first saw the girl there was asymmetry of the face, with swelling. Many of her teeth had been extracted because the lesion was impinged upon by the teeth. Both upper and lower teeth were crowded. No one seemed to know what she had, but she had been to a surgeon, who said that the jaw must be resected.

DR. CASTLEMAN: At that time, Dr. Weisberger gave me one of the slides of the original biopsy. I thought the lesion was a benign lesion; it contained fibrous tissue and bone trabeculae, and I said that it was consistent with fibrous dysplasia of the bone. The girl went home without any further treatment and returned about a year later, with evidence that the lesion had increased in size. At that time Dr. Weisberger decided to take another biopsy.

CLINICAL DIAGNOSIS

?Fibrous dysplasia of mandible.

DR. KURT H. THOMA'S DIAGNOSIS

?Angioma of mandible.
?Fibrous dysplasia of mandible.

ANATOMICAL DIAGNOSIS

Hemangioma of mandible.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Dr. Weisberger, would you describe the biopsy procedure?

DR. WEISBERGER: What Dr. Thoma described as happening during a biopsy of an angioma almost happened to me. For the first time in my life I have been terrified in the operating room. An incision was made in the mucosa over the alveolar crest. The mucosa was reflected, and as the periosteum was reflected over the buccal plate of bone, I ran into bleeding and the patient went into shock on the table. I used thumbs, fingers and bone wax to control the bleeding; there was a loss of about 1400 ml. of blood in a short time. Fortunately, the bleeding was controlled before ligation of the carotid artery was necessary.

DR. CASTLEMAN: On this biopsy we made a diagnosis of hemangioma (Fig. 2), and Dr. Weisberger later resected the tumor. The tumor was very vascular, and I should call it honeycombing, Dr. Thoma. Microscopically, in some areas, there were bony trabeculae that looked like metaplastic bone, between which were vascular spaces, but in numerous other areas the tissue was dense and looked exactly like fibrous dysplasia. The slide that we received a year previously was composed of the fibrous portion of the tumor and is the reason that we did not make the diagnosis of angioma on the first biopsy. The bulk of the tumor, however, was made up of angiomatous foci. There is no question in my mind that this was an angioma and not merely a group of blood vessels in fibrous dysplasia.

FIGURE 2.

DR. WEISBERGER: I assisted Dr. Taylor in the resection of this tumor. Perhaps he has something to say about that operation.

DR. GRANTLEY W. TAYLOR: Our thoughts on the

ward were similar to those of Dr. Thoma, although perhaps not quite as scholarly and exhaustive. Dr. Weisberger's report of massive bleeding on biopsy was certainly diagnostic, so with foreknowledge of the problem we ligated the external carotid artery at the outset and carried out the resection of the tumor without any undue difficulty, transecting anterior to the lesion. We transected through the neck of the mandible above the mass. So far as I know there were no complications of the operation; the patient has an excellent function and not a bad deformity.

DR. CASTLEMAN: I suppose that over the years the angioma had stimulated connective tissue, which then became metaplastic new bone. This must have been going on for a long time to produce this new-bone formation. I do not think the trabeculae are merely the remains of normal mandible.

CASE 42022

PRESENTATION OF CASE

First admission. A fifty-six-year-old woman entered the hospital because of vaginal bleeding.

Five years before admission, the menstrual periods became profuse. A year later, a diagnosis of "fibroid uterus with bleeding" was made at another hospital. Because of heart disease, the patient was given ten x-ray treatments to the pelvis in preference to surgery. Subsequently, the flowing ceased, but a marked radiation reaction with ulceration of the suprapubic skin, diarrhea and bladder symptoms appeared. However, all symptoms except for mild nocturia eventually cleared. She was then essentially well until six months before admission, when she had the first of three episodes of vaginal spotting.

A heart murmur had been discovered when she was thirty years old. While she had menorrhagia she experienced dyspnea on exertion. She had taken digitalis occasionally. One and a half years before admission she was told that the blood pressure was 220.

Physical examination revealed cardiac enlargement with the apical impulse 11 cm. to the left of the midline in the fourth intercostal space. A high-pitched, Grade 3 systolic murmur was heard over the entire precordium, but best in the third left intercostal space, and was transmitted to the neck. There was marked radiation change of the lower abdominal wall. Pelvic examination revealed a large, broad cervix with a polypoid cystic area on the posterior lip. A large mass was palpable behind the cervix. The blood pressure was 190 systolic, 95 diastolic.

Examination of the urine was negative. The hemoglobin was 12 gm. per 100 ml. An electrocardiogram was within normal limits. An x-ray film of the chest showed a slightly enlarged heart. Two vaginal smears were negative for tumor cells.

The patient was digitalized. A dilatation and curettage revealed the presence of a large submucosal leiomyoma. No endometrium was obtained. A cervical polyp was excised. She was discharged after a week on digitalis.

Second admission (six years later), because of intense vulvar itching of three months' duration. Since discharge there had been no more vaginal bleeding, and vaginal smears were repeatedly negative for carcinoma. Three years before admission the patient was found to have diabetes, which was controlled with 30 units of protamine zinc insulin daily.

On physical examination the cardiac findings were unchanged. The vulva was acutely inflamed. The blood pressure was 180 systolic, 90 diastolic.

Urinalysis was negative except for a yellow-brown reaction for sugar. The white-cell count was 6500, and the hemoglobin 11.8 per 100 ml. A fasting blood sugar was 167 mg. per 100 ml.

The patient was treated with boric acid compresses and sedatives and was discharged four days after admission.

Final admission (twenty-one months later). Some time after discharge, she began to have severe aching pains in the epigastrium and in both upper quadrants of the abdomen. The pains sometimes radiated to the back, usually appeared immediately after eating and lasted for several hours. They were relieved by aspirin, but not by food or alkali. The appetite became poor, and food intake was further decreased because of the possibility of precipitating pain. There was a weight loss of 10 to 15 pounds in the past year. Six months before admission, a gastrointestinal series showed a mild gastroduodenitis, and a Graham test revealed a well functioning gall bladder containing many stones. Over the past few months the abdomen began to swell. Three weeks before admission the patient noted that the urine had become quite scanty and dark. The stools were black because of iron ingestion, and when she stopped taking the iron, they became normal in color. One week before admission she began to pass several watery, nonbloody stools a day. Swelling of the ankles also developed. She never had any sharp or colicky right-upper-quadrant or shoulder pain, nor had she had any vomiting or hematemesis. There was no history of alcoholic intake. There were no significant cardiac or respiratory symptoms except for slight dyspnea on exertion.

Physical examination revealed a jaundiced, thin woman who appeared chronically ill. The cardiac examination was essentially unchanged. Moist rales were heard in both lung bases. The liver edge was palpable 3 fingerbreadths below the right costal margin. Overlying the liver a firm, freely movable nodule that descended with respiration was felt. The spleen was palpable 1 fingerbreadth below the left costal margin. (The patient's physician stated that the spleen had been palpable for at least nine months and the liver for a longer time.) The abdomen was

protuberant, and a fluid wave was present. Pelvic examination of the vagina was negative, and the uterus was not remarkable except for a mass in the right vault. (The examiner stated that the same mass had been palpable on previous admissions.) There was + + edema of the lower extremities.

The temperature was 97°F., the pulse 72, and the respirations 20. The blood pressure was 190 systolic, 80 diastolic.

The urine had a specific gravity of 1.012, was amber and gave a + + + test for bile, a + test for albumin and a negative test for sugar. Examination of the blood revealed a white-cell count of 3700, with 83 per cent neutrophils. The platelets appeared decreased. The hemoglobin was 10.2 gm. per 100 ml. The fasting blood sugar was 73 mg., the albumin 3.9 gm., the globulin 1.5 gm., and the bilirubin 4.5 mg. per 100 ml. and the alkaline phosphatase 51.1 units. A blood Hinton test was negative. The prothrombin time was 25 seconds (normal, 13 seconds). Cephalin flocculation was negative in twenty-four and forty-eight hours. The urinary urobilinogen was 0.86 Ehrlich units. A stool specimen was yellowish gray and gave a + guaiac test. An electrocardiogram was reported as suggesting left ventricular hypertrophy. X-ray films of the chest showed left ventricular hypertrophy, a high diaphragm and minute amounts of fluid in the pleural cavities. A gastrointestinal series suggested widening of the duodenal loop. There was no constant deformity of the duodenal mucosa or evidence of ulceration. The esophagus and stomach were normal. There were slight splenomegaly and hepatomegaly. Multiple stones were seen in the gall bladder, and several lay in the regions of the common and cystic ducts.

On Hykinone, the prothrombin time was reduced to 12 seconds, and the patient was digitalized. On the fourth hospital day an operation was performed.

Differential Diagnosis

Dr. John Homans, Jr.*: It seems to me unlikely that a malignant tumor, originally causing the bleeding and suppressed by the x-ray treatment, could have regrown and caused the final illness. There also seems to have been little evidence that a malignant tumor arising subsequent to and possibly stimulated by the x-ray treatment was present. The heart disease, which was mild, with an aortic murmur and slightly enlarged heart, is not important to the story. The diabetes, which became quite mild when the patient was on a restricted diet, is also, I believe, not contributory.

At the age of sixty-seven, she began to have epigastric aching, anorexia and weight loss. Food intake was further decreased because of the fear of precipitating pain. In the few months before admission, ascites developed, and three weeks before admission, it may be assumed that jaundice began. It is to be noted that there were no symptoms suggestive of gall-bladder colic and that there was no history of alcoholic intake. These symptoms as a whole certainly suggest a malignant process involving the intestinal tract directly or indirectly. Cirrhosis of the liver is also suggested but is rendered unlikely by subsequent findings.

The important findings on physical examination were jaundice, an enlarged liver and spleen, ascites, the presumably unchanged pelvic mass and + + edema of the lower extremities.

Laboratory examinations demonstrated bile and urobilinogen in the urine and depression of the formed elements of the blood with leukopenia, decreased platelets and moderate anemia. I can only explain the normal fasting blood sugar on the basis of starvation. The albumin was slightly decreased, but the globulin was low, not high. The bilirubin was elevated, and the alkaline phosphatase was very high. The prothrombin time was elevated, but it is to be noted that it returned to normal on Hykinone therapy, indicating that the liver function was not seriously deranged. Cephalin flocculation was negative.

May we see the films, Dr. Hanelin?

Dr. Joseph Hanelin: The chest films show the high diaphragm, clear lung fields and a small amount of fluid at either base, somewhat greater on the left.

From the gastrointestinal examination there is evidence of localized impingement upon the medial aspect of the duodenal loop as well as some broadening of the loop itself. Multiple opaque calculi are present within the gall bladder, and there is also indication of biliary stones lying in the region of the cystic duct and proximal end of the common duct. The gall bladder is probably enlarged in view of the wide separation between the stones in the region of the cystic duct and fundus of the gall bladder. Extrinsic pressure upon the lateral aspect of the duodenal loop could result from the enlarged gall bladder. Diffuse haziness over the abdomen and bulging of the flanks are consistent with ascites.

Dr. Homans: Can you tell us more specifically the nature of the process deforming the duodenal loop?

Dr. Hanelin: It is impossible to be certain of the nature of the lesion. Similar appearances have been noted with carcinoma of the head of the pancreas, tumor of the ampulla of Vater, stone in the common duct and even metastasis to the pancreatic head.

Dr. Homans: To begin with, I can dismiss the possibility of cirrhosis of the liver. The liver-function tests are entirely in the direction of an obstructive cause for the jaundice. There was no history of alcoholism, and this diagnosis would ignore the x-ray findings in the vicinity of the pancreas. There was no evidence from the history of acute or recurrent pancreatitis. I do not see how the gallstones alone could account for the picture, for there would then

*Assistant in medicine, Massachusetts General Hospital.

be no explanation for the ascites. The x-ray examinations seem to rule out carcinoma of the stomach. I am still impressed that this is a story of a neoplastic disease. Could it have been carcinoma of the gall bladder? This disease usually occurs in the presence of stones, and the gall bladder is said to have been enlarged. This finding, however, could just as well be explained by a hydrops as the result of blockage by a stone. Again unexplained would be the enlargement of the duodenal loop unless, as Dr. Hanelin suggested, it could represent a metastasis to this area. The diagnosis of a retroperitoneal tumor with extension to the pancreas or of a pelvic tumor with extension to this area seems possible though there is no way of getting direct evidence for either.

I am left with the perhaps too obvious diagnosis of carcinoma of the head of the pancreas or ampulla of Vater. Carcinoma of the head of the pancreas certainly fits the clinical symptoms of the patient's last illness and is consistent with the x-ray and laboratory findings. Carcinoma of the ampulla of Vater is also a possibility though with this I should have expected more than the mention of a single positive guaiac test. The presence of urobilinogen in the urine indicates that the obstruction was not complete. This could be explained by incomplete blockage of the common duct, by a tumor in these areas or by metastases in the liver. The last seems most likely. I think that there had been metastatic spread to the peritoneal cavity to account for the ascites. The small amount of pleural fluid may have been secondary to this. The enlarged spleen may be explained on the basis of extension to involve the splenic vein. I expect that the blood findings were secondary to the enlarged spleen and that the edema of the legs was due to a combination of the ascites and inactivity. There could have been, however, metastatic involvement of the splenic veins.

My first diagnosis would be carcinoma of the head of the pancreas with peritoneal and liver metastases. Carcinoma of the ampulla of Vater would be second, and carcinoma of the gall bladder would be least likely.

DR. WINFIELD S. MORGAN: Dr. Harwood, you followed this patient; have you any comments?

DR. REED HARWOOD: During the time that she was under my care the diabetes was easily controlled on 30 units of NPH insulin daily.

The problems that I had to treat during the period between the second and third admissions were "nervousness" and "indigestion." On the very first visit to my office, she complained of "gas" and vague abdominal discomfort. This symptom fluctuated with her state of mind and at times was ameliorated by such medications as belladonna and phenobarbital. On some visits, this complaint was absent or much improved. The state of her nervousness also fluctuated. For the most part she seemed extremely tense, and she spoke in a trembling voice and gave other evidences of anxiety. Five months before the final admission the abdominal symptoms seemed to take ascendancy over the nervous ones, and she began to complain of a general "gnawing" and dull aches rather poorly localized. The x-ray studies performed by Dr. Harvey R. Morrison six months before admission were reported as follows: "The stomach emptied at a fairly normal rate through a duodenal cap that appeared normal, aside from coarsening of the rugal pattern. The coarsening extended down along the descending duodenal loop to about its midportion, where the mucosal relief became normal." I have since reviewed these films carefully with Dr. Morrison, and we were unable to find any widening of the duodenal loop.

Since the gastrointestinal series was essentially normal and since it seemed unlikely that the complaints were caused by the many gallstones, I decided that it would be reasonable to let the patient go to Canada to visit some relatives. On her return she reported that she had had a miserable summer, with "gas" and general soreness of the abdomen. At this time there was questionable icterus of the scleras and a suggestion of ascites. Arrangements were made at once for her to be admitted to the hospital, and in the intervening six days deep jaundice and marked ascites had developed.

I would be interested in Dr. Castleman's opinion about when the disease actually began.

CLINICAL DIAGNOSIS

Carcinoma of pancreas.

DR. JOHN HOMANS, JR.'S, DIAGNOSIS

Carcinoma of head of pancreas.

ANATOMICAL DIAGNOSES

Adenocarcinoma of pancreas, with metastases to regional lymph nodes, lungs and adrenal glands and obstruction of common bile duct.

Cholangitis, acute and chronic, with abscess formation.

Thrombosis of hepatic veins, with focal infarction.

PATHOLOGICAL DISCUSSION

DR. MORGAN: Dr. Bartlett, will you tell us your preoperative diagnosis and findings at operation?

DR. MARSHALL K. BARTLETT: We, too, had decided that the most likely diagnosis in this case was carcinoma of the pancreas. When the peritoneal cavity was opened, considerable ascitic fluid was encountered, and an estimated 3 or 4 liters was removed. There was a hard mass involving the entire head of the pancreas and infiltrating the retroperitoneal tissues, to which it was fixed. There was considerable edema surrounding the mass, and the entire tail of the pancreas was nodular. The entire venous system in the portal area was engorged. The

gall bladder was distended and when emptied proved to contain dark bile with multiple faceted, pigmented stones, all less than 1 cm. in diameter. The common duct was much dilated, and there was a good deal of edema and venous engorgement over its surface. No metastases were felt in the liver, which appeared essentially normal. The stomach and duodenum were normal to palpation except for some edema of the wall and the dilated veins already mentioned. There were extensive omental adhesions in the pelvis, and palpation was unsatisfactory. It was decided to do the simplest procedure that offered a chance to relieve the jaundice, and, consequently, an anastomosis was made between the gall bladder and the duodenum. A needle biopsy of the head of the pancreas was taken.

DR. MORGAN: The needle biopsy confirmed the gross impression of carcinoma. The condition of this patient during the first few days after operation was fairly good, but on the fifth postoperative day the temperature rose to 103.5°F. and jaundice increased. The lungs and kidneys were ruled out as sources of infection, and it was believed that an acute cholangitis probably accounted for the fever. The septic course continued despite Chloromycetin therapy, jaundice deepened, the ascites reaccumulated, and after several days of stupor she died on the twentieth postoperative day.

At autopsy the peritoneal cavity contained 800 ml. of bile-stained fluid, and the operative site was in good condition. Most of the pancreas was replaced by a firm, white tumor, which extended to involve adjacent structures, including part of the left adrenal gland. Microscopically, this tumor proved to be a fairly well differentiated adenocarcinoma. Although there were metastases to the mesenteric lymph nodes there were none to the liver or peritoneum. The portal vein, although not occluded, was markedly narrowed by tumor, and I believe this may in part have accounted for the ascites. The ampulla of Vater and the distal portion of the common bile duct were normal, but immediately distal to the junction of the hepatic and cystic ducts tumor had surrounded and invaded these structures and completely occluded the common bile duct at this level. Proximally, the cystic duct and the hepatic ducts, with their intrahepatic ramifications, were dilated up to 1.5 cm. The liver weighed 2000 gm.; scattered throughout it were many abscesses ranging up to 2 cm. in diameter.

Microscopical sections revealed a severe acute and chronic cholangitis with abscess formation and much destruction of liver parenchyma in which colonies of bacteria were frequent. In addition, there were a considerable number of areas of necrosis showing little inflammatory response, and these were interpreted as foci of infarction. To go along with this we found that a number of the veins contained septic thrombi.

The heart weighed 330 gm. and exhibited mild to moderate old rheumatic involvement of the aortic and mitral valves. The lungs were generally clear except for a single small metastatic lesion. The endometrium was atrophic, consistent with the age of the patient, but was otherwise not remarkable, and the uterus contained several intramural and subserosal leiomyomas measuring up to 5 cm. in diameter.

There was no evidence of hyalinization of the pancreatic islets or diabetic glomerulosclerosis in the kidney to go along with the diabetes mellitus. The spleen was somewhat heavy, weighing 440 gm., but microscopically showed only congestion. A second white-cell count done before operation was 6000 so that I do not believe this patient really had a leukopenia and there were no tumor metastases to bone.

DR. BENJAMIN CASTLEMAN: It is really impossible to answer Dr. Harwood's question about when the carcinoma actually began. I should guess that it was between one and a half and two years before she died — that is, when the symptoms of epigastric and back pain developed.

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UNIVERSITAS TUFTENSIS

AN American university, according to a somewhat abbreviated definition, is an institution equipped to prosecute original research in connection with professional schools. By such an interpretation Tufts College, the seventh institution of higher education to be founded in Massachusetts and the sixteenth in all New England, became in fact a university with the establishment of its medical school in 1893.

This was Tufts College's first graduate school; an undergraduate engineering course had already been developed in 1865, the year that Massachusetts Institute of Technology opened its doors; a school of religion—later the Crane Theological School—was established in 1869; and in 1892 women were admitted to a division that was ultimately chartered as Jackson College. The gradual development of new units continued so that in 1955 the total establishment consisted of 4 undergraduate colleges—those of liberal arts and of engineering, Jackson College for Women and a college of special studies; and 5 graduate schools—Crane Theological School, the Graduate School of Arts and Sciences, the Fletcher School of Law and Diplomacy, and the schools of medicine and dental medicine.

This is the institution, known best to many of the *Journal's* readers because of its school of medicine, that was chartered in 1852, in a period of strict orthodoxy, with the provision that no particular religious opinions were ever to be required of its officers or students. The movement leading toward its establishment had started early in the century, and by the fourth decade funds were already being raised for the realization of the project. Religious liberalism was on the move, but as yet Harvard alone of the New England colleges had accepted liberal doctrines and had become essentially a Unitarian institution. Somewhat more cautiously a Universalist group had decided that another liberal but not a radical school should be established, and it was this group that carried forward the founding of the new college.

Its location on a hill in Medford near the Mystic lakes and the Mystic River was decided by a gift of land from Charles Tufts, of Charlestown, a landowner and successful manufacturer, and it was for him that the college was named. The first president was Hosea Ballou, II, an overseer of Harvard, and the cornerstone of Ballou Hall, still the administrative center of the college, was laid in 1853. Students were enrolled in the following year, and just a hundred years ago the first group of freshmen was at its classes.

The name Tufts College, sanctioned as it has been by tradition and appropriate as it remained for the undergraduate departments, became more and more paradoxical and confusing in its application to an institution of learning that had been fulfilling the destiny of a university for half a century. Accordingly, early in 1955, the trustees of Tufts College petitioned

the Board of Collegiate Authority of the Commonwealth for permission "to use the name University in referring to the institution as a whole and particularly in designating its graduate and professional schools." This permission became a matter of official record on March 22 and in due course was celebrated by a University Convocation held at the College on December 8. On this occasion President Wessell defined to the delegates and guests the function of Tufts: to be and to develop as a small university of high quality, doing a few carefully selected things well and not attempting "to be all things to all men."

The part of Tufts University School of Medicine in this development has been a distinguished one. Growing steadily in prestige under a succession of able leaders, it is one of a reciprocating triad of schools that, in conjunction with the hospitals with which they are integrated, have made Boston one of the leading medical centers of the world.

EMERGENCY MEDICAL CARE

THE inability to locate a physician in an emergency is regarded by certain segments of the public as evidence that local medical care is inadequate. On many occasions, irate citizens, apparently unable to obtain a physician for emergency medical care, have written to the Society and newspapers arguing that socialized medicine is the answer. Once medicine is socialized, they reason, there will be no problem getting a doctor in a hurry.

So great was the hue and cry over emergency medical coverage that a bill was filed in the Legislature a few years ago calling for an investigation of emergency medical coverage in the Commonwealth.

In metropolitan areas throughout Massachusetts, several complaints of nonavailability of physicians for emergency medical care were widely publicized. Investigations by the Society revealed that most of the complaints were completely unjustified, or grossly exaggerated. Some of them were not publicly answered by the Society because investigation uncovered circumstances that, if reported, would have been highly embarrassing to the complainant.

In the smaller communities, providing emergency medical coverage poses no particular problem. Most residents in these communities have a family physician who, when he knows he will not be available, makes arrangements for coverage of his patients.

In cities, however, the problem is many times magnified. City dwellers apparently think that they have a right to an emergency doctor despite the fact that before and after the emergency, they have no allegiance to a family physician. Consequently, no physician feels personally responsible for their welfare.

Whether or not a person has a "right" to immediate medical coverage and whether or not a physician is morally (he is not legally) obligated to answer emergency medical calls from absolute strangers are academic questions.

Nevertheless, the medical profession has assumed the responsibility of providing emergency medical coverage, and since 1950, several plans have been put into operation throughout the Commonwealth. Several communities had systems set up in the 1940's.

Types of service plans range from those handled from a hospital switchboard to a more elaborate and expensive system, such as the one that covers Boston and Brookline. A private telephone-service exchange handles this call plan, financed proportionately by the Suffolk, Norfolk and Middlesex South District medical societies.

The Commonwealth, if not completely, is now adequately covered by plans for emergency medical calls set up and operated by the medical profession. Complaints from the public have become few and far between.

Complaints from the physicians involved in such plans, however, are on the increase.

Most of the "emergency" calls are not real emergencies. One physician reported that three of his last four calls, all in the early dawn, were occasioned by a chronic mental disease, a minimal case of asthma and a 1.5-cm. laceration of the nose, and on the fourth, another physician had answered the call.

Many citizens expect free emergency coverage. In the Boston area, physicians have been called to treat drunken persons, dope addicts and pranksters. A few of the physicians have been manhandled and robbed. And streets are not properly identified, house numbers are missing, and street lighting is inadequate.

Despite the fact that he may find that answering emergency medical calls is often needless, hazardous, annoying and frustrating, the physician, by participating in a plan for emergency medical-calls in his community, is performing a valuable public service.

The faults of the systems are human faults. The layman cannot be expected to determine what is or what is not a true emergency. If a physician does not arrive within five minutes, one can understand why the layman telephones frantically for another physician. Some people will never pay a physician, emergency call or not. Others do not believe in having a family medical adviser. And, apparently, as long as there are people, there will be addicts, drunkards and pranksters.

Those are faults with which the physician will have to live if he is to be of service to the few patients in need of immediate and necessary emergency medical treatment.

PREVENTION OF ACUTE GLOMERULONEPHRITIS

THE late Dr. Warfield T. Longcope and his associates at the Johns Hopkins Hospital exhibited a long and continuous interest in the relation between infections due to the hemolytic streptococcus and acute glomerulonephritis. In 1942 Williams, Longcope and Janeway[1] reported the results of a comparative study on the course of acute hemorrhagic nephritis in two groups treated in the same manner except that one group was given sulfanilamide. Most of the patients were followed for two to five years or longer. The results indicated that in the subjects receiving sulfanilamide the foci of infection had cleared up more rapidly, the signs of renal damage had disappeared more promptly, the exacerbations of nephritis after tonsillectomy occurred less frequently, the duration of the edema and hypertension was shorter, and the clinical recoveries were more complete. These results were interpreted as being due to the bacteriostatic effect of sulfanilamide, since the streptococci were not eliminated from the tonsils by the sulfonamide and the antistreptolysin titers were practically the same in both groups.

In commenting on these effects the authors considered that they may not have achieved optimum results because of the brief period of treatment. They suggested, therefore, that it may be desirable to institute during convalescence a form of continuous therapy with sulfonamide similar to that which seemed to be successful in preventing recurrences of rheumatic fever. They expressed the intention of adopting such a procedure over long periods after the acute phase of the disease and hoped thereby to shorten the duration of the kidney disease, prevent recrudescences of infections with hemolytic streptococci and increase the number of final recoveries.

It is not known whether these objectives were achieved, but since that time many physicians have considered acute nephritis, like rheumatic fever, an indication for continuous prophylaxis. This is particularly so since penicillin became available and it was shown that treatment with this antibiotic, if continued for at least seven to ten days, will eradicate Group A streptococci from carriers and that continuous daily administration orally, or repeated and properly spaced injections of long-acting depot preparations, would prevent infections with this group and the consequent recrudescences of rheumatic fever. Theoretically, similar methods should be equally effective in the prevention of acute nephritis, but because of certain fundamental differences between the two complications, it seems necessary to alter this preventive program. This was pointed out by Rammelkamp[2] in a review of the subject at the 1955 meeting of the American College of Physicians.

It has recently been shown that only certain strains of Group A streptococci are capable of initiating acute nephritis. In this country, such nephritogenic strains belong to Lancefield's Type 12, but strains of Types 4 and 25, as well as a new strain, named Red Lake, may produce this complication. Thus, the serologic identification of the infecting strain in streptococcal infections becomes an important laboratory procedure.

In one controlled study carried out during an epidemic of infections with Type 12 streptococci it was shown that the administration of penicillin early in the course of the disease reduced the frequency of renal complications, but the results were not so dramatic as those in similar studies designed to prevent rheumatic fever. The failure to prevent renal damage in every patient receiving penicillin may have been due to the short latent period in many patients in whom nephritis developed; the importance of early treatment and possibly the need for other preventive measures were brought out in that study.

After infection with most nephritogenic types of Group A streptococci, the attack rate of acute nephritis is considerably higher than that of rheumatic fever, and, as a result, epidemics of nephritis in families and in small communities have frequently been observed. Such epidemics, according to Rammelkamp,[2] can be prevented. He recommends that, for persons coming into intimate contact with a patient with acute nephritis, proper cultures should be made, and those shown to harbor beta-hemolytic streptococci should receive an injection of 600,000 units of benzathine penicillin. The causative organism can thus be limited in its spread within the family or other population group; only in this way can the incidence of nephritis be reduced appreciably. He considers it entirely reasonable to recommend that acute nephritis be made a reportable disease so that the public-health authorities may assist in the development of effective control measures.

The problem of prevention of *recurrent* attacks of nephritis differs, however, from that of recrudescences in acute rheumatic fever. In this respect the patient with chronic nephritis must also be distinguished from the one with acute glomerulonephritis. In the former acute exacerbations may develop soon after the onset of any of a variety of acute infections. Characteristically, no latent period is discernible and such an exacerbation may precipitate an episode of renal failure. Rammelkamp[2] therefore considers it advisable to place patients with signs of chronic nephritis on a prophylactic regimen similar to that recommended for the prevention of rheumatic recrudescences.

Patients in whom acute glomerulonephritis develops after streptococcal infection, on the other hand, usually recover completely and fail to show an increased susceptibility to recurrent attacks. In fact, they may even be less susceptible to acute nephritis than normal persons, because their serum usually exhibits type-specific antibodies, which may

persist for several years. Persons with such antibodies to the nephritogenic type have been shown to be resistant to infection with the homologous type of streptococcus, although normally susceptible to infection by other types, but the latter will not precipitate new attacks of nephritis in these patients. The patient recovering from acute nephritis, therefore, should not require protection from streptococcal and other bacterial infections.

Rammelkamp[2] goes on to emphasize the need for further knowledge of the immune status of the patients who have had acute nephritis, particularly when the majority of such patients will have received penicillin during the acute attack or for the antecedent streptococcal infection. Such therapy, he points out, may inhibit type-specific antibody formation, even though administered as long as ten days after the onset of the streptococcal infection. It is thus possible that in some a second attack due to one of the nephritogenic streptococci will develop, and that second attacks of acute nephritis will be observed, although no case has yet been described.

References

1. Williams, R. H., Longcope, W. T., and Janeway, C. A. Use of sulfanilamide in treatment of acute glomerular nephritis. *Am. J. M. Sc.* **203**:157-172, 1942.
2. Rammelkamp, C. A. Prevention of acute nephritis. *Ann. Int. Med.* **43**:511-517, 1955.

AMORY PRIZEMEN

Having announced in January, 1955, the opportunity for candidates to apply for the third group of Francis Amory Septennial Prizes awarded in Boston by the American Academy of Arts and Sciences, the *Journal* now takes pleasure in announcing the results of the judging. The prizes are specifically designated "for outstanding work addressed to the alleviation or cure of diseases affecting the human reproductive organs, in particular those of man."

The seven prizes of $3500 each for work completed in or before November, 1954, were awarded last October as follows:

To Frederic E. B. Foley, Lowry Medical Arts Building, St. Paul, Minnesota, for outstanding inventive and surgical genius productive of numerous contrivances, instruments and operations of great value in the treatment of those afflicted with urological disease.

To Choh Hao Li, University of California, Berkeley, California, for his work on the relation of the anterior pituitary hormones to the maintenance and functioning of the human reproductive organs.

To Thaddeus R. R. Mann, Molteno Institute, University of Cambridge, Cambridge, England, for his basic contributions to the rapidly expanding field of the biochemistry of reproductive functions providing basic data stimulating research and clinical progress.

To Terence J. Millin, The Queen's Gate Clinic, London, England, for his valuable contribution to surgery by devising and developing the technique of retropubic prostatectomy for benign hyperplasia of the prostate and for adapting this technique to radical prostatectomy and vesiculectomy for the cure of cancer of the prostate.

To Warren O. Nelson, State University of Iowa, College of Medicine, Iowa City, Iowa, for his penetrating studies of the structural relationships of the male sex organs and of the factors that determine the functional activities of the various components thereof.

To Frederick J. Wallace, American Cystoscope Makers, Inc., New York, N. Y., for his cooperation with the urological profession in developing diagnostic and therapeutic instruments which have contributed materially to the technical advances in this specialty.

To Lawson Wilkins, Johns Hopkins University, Baltimore, Maryland, in recognition of his significant contributions to fundamental knowledge of growth and development of secondary sex characteristics in man and his brilliant application of adrenal cortical hormone to their management and treatment.

The Communication was delivered by Amory Prizeman Terence J. Millin, of London, on the impact of the Amory Prize researches in medicine and in other fields.

SUPPORT FOR THE MARCH OF DIMES

The annual appeal of the National Foundation for Infantile Paralysis for funds to support its activities in 1956 is to go on through the month of January. The people of New England, and particularly those of Massachusetts, have special cause for feeling an intimate interest in contributing to this year's March of Dimes. During 1955, when Massachusetts suffered the worst poliomyelitis epidemic in its history (or since 1916), a significant, if not major, proportion of the support for the modern care that was afforded the victims of this disease came directly from the National Foundation for Infantile Paralysis. Moreover, many outstanding research projects conducted in this area, including those that made possible the cultivation of the poliomyelitis viruses and the preparation of vaccines for immunization, have received substantial support from contributions to the March of Dimes. Some of the ways in which these funds have been of help directly to New England are detailed by Dr. Van Riper elsewhere in this issue of the *Journal*.

The physicians and citizens of Massachusetts and of all New England, although vitally interested, of course, in the health and welfare of the people of this area, have always been equally if not more interested in the welfare and health of people everywhere. It is in this spirit, rather than as a reward for benefits received, that they should consider the March of Dimes a worthy cause to support personally and to encourage their patients and friends to do likewise. The numerous ways in which the March of Dimes has helped and continues to support fundamental researches in poliomyelitis, in viral diseases and in many other important health areas, as well as the appreciation of the many more direct benefits to victims of poliomyelitis throughout the United States, should provide ample reason for a generous response to its appeal.

Among the conditions over which nux vomica, and its active principle, strychnia, possess most useful powers, is that of habitual constipation, from muscular atony of the intestinal tube.

Boston M. & S. J., *Jan. 17, 1855*

MASSACHUSETTS MEDICAL SOCIETY

STATED MEETING OF THE COUNCIL

A stated meeting of the Council will be held in the John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, February 1, at 10:30 a.m.

Business:

1. Call to order at 10:30 a.m.
2. Presentation of record of meeting held October 5, 1955, as published in Vol. 253, Supplement No. 2, November 17, 1955, of the *New England Journal of Medicine*.
3. Reports of standing and special committees.
4. Such other business as may legally come before this meeting.

ROBERT W. BUCK, M.D.,
Secretary

COMMITTEE ON MATERNAL WELFARE

RUPTURE OF AORTIC ANEURYSM

A twenty-five-year-old gravida I, para 0, died in labor at term suddenly and without warning after a most extraordinary prenatal course.

At about seven weeks she was admitted to the hospital in deep shock and was operated on for suspected ruptured ectopic pregnancy. Laparotomy revealed 2.5 liters of pus in the abdominal cavity for which meticulous exploration revealed no cause. Cultures showed staphylococcus, for which appropriate antibiotics as well as several blood transfusions were given. With careful postoperative care, she survived this experience.

She received close attention during the remainder of her pregnancy without further difficulty and was admitted to the hospital in desultory labor at term. All vital signs were normal. After twenty-four hours active labor began. The cervix was tightly closed. She received 100 mg. of Demerol, 90 mg. of Seconal and a small dose of scopolamine. During the next four hours, the cervix began to change and another 100 mg. of Demerol was given, after which she fell asleep; satisfactory progress continued in an individual room. An attendant arranged the bedcovers at 1:47 a.m. and left, returning thirty-five minutes later to find the patient dead.

Autopsy revealed the rupture of an aneurysm of the aorta into the left pleural space, which was now filled with blood, and, in addition, an unruptured aneurysm of the left common iliac artery. There were no other morphologic findings at autopsy, nor anything that in retrospect might have explained the suppurative peritonitis found in the first trimester.

Although this death was obviously nonpreventable, comment is warranted regarding the mysterious peritonitis, which was presumably of pelvic origin. Could this have originated in the tubes? At any rate, skillful care saved the patient's life, which was later lost because of aneurysms in a normotensive patient. Vascular changes, especially those involving arterial walls, are receiving more and more attention as phenomena caused by pregnancy. But with current clinical tools of diagnosis and treatment, the death was truly nonpreventable. On the other hand, this woman was in labor and should never have been left unattended. Furthermore, she was under narcotics and scopolamine, a desirable combination in labor but one notorious for producing irrational and sometimes violent behavior. It was therefore considered unfortunate that this patient was left unobserved from 1:47 until 2:20 a.m., when she was found dead.

JOHN FIGGIS JEWETT, M.D.
Chairman

SICK LEAVE AT BOSTON NAVAL SHIPYARD

The following letter has been received from the secretary of the Charlestown Metal Trades Council:

Dr. Robert W. Buck, Secretary
Massachusetts Medical Society
22 Fenway
Boston, Massachusetts

Dear Sir:

On Tuesday evening, December 13th, 1955, an article appeared in the Boston Traveler relating to alleged abuses of sick leave by employees of the Boston Naval Shipyard.

This is of grave concern to us because the Charlestown Metal Trades Council is an organization composed entirely of A.F. of L. Craft Unions in the Shipyard.

The Council and it's member local unions have had many discussions with management on the problem of sick leave in the Shipyard.

We were shocked by the article referred to above, which seemed to imply that the members of the Medical Association in the Boston area were deliberately falsifying sick leave forms for Boston Naval Shipyard employees and thereby contributing to a substantial abuse of this privilege.

We feel this implication is wholly unwarranted.

Any responsible individual and organization must recognize that in any large group such as the 10,000 employees in the Boston Naval Shipyard, a very small minority will take advantage of any privilege, but it is also true that any responsible individual or organization should not allow abuse by a minority to result in restrictive action against the majority.

As stated above the Charlestown Metal Trades Council has discussed this problem with Shipyard management. Three months ago the Council made a series of specific recommendations, which we felt would correct sick leave abuses. We were assured that these recommendations would be given careful consideration, further at that time, the Shipyard Commander stated that he was considering writing a letter to your society pertaining to this problem.

However we were assured that no action would be taken until we had an opportunity to discuss all aspects of this problem further.

In the light of the above, we feel certain that you will understand the feeling of shock and resentment caused by the release of the letter to your society. We feel that this is a management problem within the Shipyard and that an attempt to create an unhealthy atmosphere of suspicion between doctors and their patients is not the proper approach to the problem.

HENRY A. WOZNIAK
Secretary

ROBERT W. BUCK, M.D.
Secretary

DEATH

STRATTON — Ralph R. Stratton, M.D., of Melrose, died on November 27. He was in his eighty-first year.

Dr. Stratton received his degree from Harvard Medical School in 1902. He was chief surgeon and chairman emeritus of the medical board of Melrose Hospital and a member of the advisory committee of the hospital's School of Nursing, past president of the Middlesex East District Medical Society, a member of the Council and chairman of the Committee of Ethics and Discipline of the Massachusetts Medical Society, and a fellow of the American Medical Association.

He is survived by his widow and a son.

CORRESPONDENCE

POLIOMYELITIS AHEAD: THE REASONS BEHIND THE 1956 MARCH OF DIMES IN NEW ENGLAND

To the Editor: How did the March of Dimes help New England meet its poliomyelitis epidemic last summer? This is a pertinent question today when New England physicians are being asked to support the January, 1956, March of Dimes.

The attack rate in the New England states in 1955 was the highest in the nation. In Massachusetts, where 3856 cases were reported through November 26, the rate was over six times as high as the average of the previous five years.

Significant increases in the 1955 rates and absolute numbers of cases over the averages of the previous five years were recorded in all the New England states, though none were so high as Massachusetts. We shall therefore take Massachusetts as the example of epidemic aid rendered by the National Foundation for Infantile Paralysis. Similar aid, though in lesser amount, was given to all the other New England states in 1955.

To help Massachusetts meet the largest poliomyelitis epidemic in its history, the National Foundation for Infantile Paralysis, using March of Dimes funds raised in 1955 and earlier years, gave the following important services (in the first eleven months of the year):

Supplied 755,000 cc. (over $700,000 worth) of gamma globulin to provide temporary protection against paralytic poliomyelitis.

Supplied emergency aid in dollars — in the amount of $170,125 — from national headquarters to 7 local chapters to pay for care of patients.

Sent shipments of emergency equipment — namely, 145 tank respirators, 69 chest respirators, 64 hot pack machines and 65 rocking beds.

Arranged for the recruitment of 18 physical therapists, 59 nurses and 7 medical social workers to work in Massachusetts hospitals.

Will there be poliomyelitis problems in New England in 1956? Unquestionably, yes. Some will be the aftermath of the 1955 epidemic or attacks in earlier years. Others will be new cases. The Salk vaccine appears to be a major weapon against paralytic poliomyelitis, but it has not yet won the war against this disease.

The following brief review of the record of the National Foundation for Infantile Paralysis in New England should further help to orient physicians to the many nonepidemic services to patients and the professions that have been made possible by the March of Dimes since 1938, when the National Foundation was established.

There are 15 local chapters of the National Foundation in Massachusetts; 16 in Maine; 14 in Vermont; 7 in Rhode Island; 10 in New Hampshire; and 9 in Connecticut.

About $5,160,000 has been spent by local chapters for the care of patients in Massachusetts, $1,050,000 in Maine, $830,000 in New Hampshire, $490,000 in Vermont, $630,000 in Rhode Island and $2,940,000 in Connecticut.

A total of 393 National Foundation scholarships and fellowships have gone to residents of Massachusetts, 30 to residents of Maine, 22 to residents of New Hampshire, 19 to residents of Rhode Island, and 100 to residents of Connecticut.

Professional-education grants, in addition, have gone to a number of New England institutions, including Boston University, the Children's Medical Center (Boston), Harvard University, Simmons College, Grace-New Haven Community Hospital and Yale University. March of Dimes grants for professional education in Massachusetts have totalled $424,000; in Connecticut, $170,000.

A vast and fruitful amount of research in virology and in the treatment of the aftereffects of poliomyelitis has been conducted in New England institutions with the help of March of Dimes grants.

About $1,400,000 in March of Dimes research grants have gone to institutions in Massachusetts, including the Boston City Hospital, the Children's Medical Center (Boston), Harvard University, the Massachusetts General Hospital, the Massachusetts Institute of Technology, the Massachusetts Medical Society and the Massachusetts Memorial Hospitals. It is significant that one Nobel-prize-winning group of research men in Massachusetts received generous March of Dimes support.

Yale University has had about $1,443,000 in March of Dimes grants for research. Grants have also been made to Brown University and the University of Vermont.

One of the 14 regional respiratory centers in the United States is located in New England. This is the Mary MacArthur Memorial Respiratory Unit in Wellesley Hills, Massachusetts. Toward the support of this center, which has achieved a high reputation for its work in respiratory physiology, the March of Dimes has contributed over $230,000.

To help New England states initiate programs of vaccination to prevent paralytic poliomyelitis the March of Dimes in 1955 gave about 201,000 cc. of Salk vaccine to Massachusetts, about 45,500 cc. to Maine, 36,000 cc. to Vermont, 42,000 cc. to New Hampshire, 69,000 cc. to Rhode Island, and 233,000 cc. to Connecticut. (The National Foundation is no longer distributing vaccine.)

The results already reported from the use of the vaccine are most encouraging, but they must not be allowed to blind the eye of the medical profession to the road that still lies ahead. There remains a great need for additional research to improve the Salk vaccine, to determine the duration of the immunity it confers (and conversely to determine the need for "booster shots") and to provide the best possible treatment for patients already or yet to be involved with paralytic poliomyelitis. There is also a vast need for the professional education of young men and women who will contribute to the necessary research and help give the needed treatment.

To pay for research, education and aid to patients with poliomyelitis, the March of Dimes needs $47,600,000 in 1956. New England physicians, knowing both the need and the record, will want to support and to urge their patients to support the 1956 March of Dimes in their own communities.

HART E. VAN RIPER, M.D.
Medical Director
National Foundation for
Infantile Paralysis, Inc.
New York City

REGARDING SALK VACCINE

To the Editor: In a letter published in the December 1, 1955, issue of the *Journal,* and the subject of editorial comment in the same issue, the Massachusetts State Polio Advisory Committee has outlined the reasons for what it calls its "*conservative approach* to the problem of mass inoculation with vaccine." The Committee also states its hope that when some additional technical information is available it may then give "unqualified approval to a poliomyelitis vaccination program in Massachusetts."

The purpose of this letter is to suggest that the volume of scientific information on the safety and efficacy of the Salk vaccine has already reached the point where any physician who administers the vaccine is fully warranted in providing this prophylactic protection for his patients. The Massachusetts State Polio Advisory Committee is to be commended for the careful study and attention it has given and is giving to the question of immunization against poliomyelitis. It must be recognized, however, that a "conservative approach" can be held too long, and in the course of progress of scientific events may no longer be the path of wisdom.

Theoretical risks from the use of Salk vaccine or any other therapeutic or prophylactic agent may be postulated, but the question must be settled in terms of factual experience.

At the 1955 annual meeting of the American Public Health Association in Kansas City, in November, a considerable amount of new information was presented to confirm the safety and efficacy of the Salk vaccine. On November 17, Dr. Leonard Scheele, Surgeon General of the United States Public Health Service, presented an "Interim Report of the Public Health Service's Technical Committee on Poliomyelitis Vaccine." The members of this committee are David Bodian, M.D., Thomas Francis, Jr., M.D., Carl Larson, M.D., Jonas E. Salk, M.D., Richard E. Shope, M.D., Joseph E. Smadel, M.D., and James A. Shannon, M.D., chairman.

The interim report of the Technical Committee appears in the December 10, 1955, issue of the *Journal of the American Medical Association.* The studies and results therein reported answer most of the specific points on the safety of the Salk vaccine that have troubled the members of the Massachusetts State Polio Advisory Committee.

It may be pointed out that the Public Health Service's Technical Advisory Committee has been in a position to follow day-by-day developments in the manufacture and testing of Salk vaccine. The members of the Committee have given a great amount of time to the study of the problems involved and their conclusions and recommendations must carry great weight.

The following summary of the Technical Committee's interim report covers and resolves the points about which there may previously have been some justified doubts:

> The Technical Committee on Poliomyelitis Vaccine is of the opinion that the principal factors that were involved in earlier manufacturing and testing difficulties have been identified and corrective measures have been taken. Among these factors is the absolute need for removal of particles within which virus may be protected from inactivation by formaldehyde. Provisions have been made to insure as far as possible the removal of such protected particles by suitably spaced filtration procedures. In addition, the safety-test program has been strengthened by improved sampling procedures in the tissue culture tests and by increasing the sensitivity of the monkey safety tests. These measures, together with continuous review of plant production records, assure the safety of released vaccine and should make possible an increased availability of vaccine.

It is to be hoped that the high degree of confidence placed in the Technical Committee's findings by physicians in 46 other states, where vaccination programs are proceeding and where in the aggregate millions of children have been vaccinated without any untoward events, will soon be reflected in Massachusetts.

It may be a point of significant interest that the American Academy of Pediatrics, on October 4, 1955, approved the following report of its Committee on the Control of Infectious Diseases:

> In view of the information made available to the Committee by the United States Public Health Service, and by others, which indicates a trend in favor of protection against paralytic poliomyelitis in recipients of poliomyelitis vaccine; in view of recent improvements in production, and in the control and testing of such vaccine; the Committee approves the resumption of vaccination against poliomyelitis in the priority age groups established by responsible authorities at state and territorial levels.
>
> The Committee commends the continuing efforts to develop further improvements in poliomyelitis vaccines and their methods of production and control; and the continuation of careful surveillance.

The American Academy of Pediatrics report, approved by its executive board, was signed by Alms C. McGuinness, M.D., chairman, Edward C. Curnen, Jr., M.D., J. Harry Ebbs, M.D., Frederick C. Robbins, M.D., Edward B. Shaw, M.D., Alex J. Steigman, M.D., and Franklin H. Top, M.D., with Philip S. Barba, M.D., Russell J. Blattner, M.D., and Joseph Stokes, M.D., as consultants.

The effectiveness of the Salk vaccine in preventing paralytic poliomyelitis is attested by the reported results of 1955 experience in many states. Even though dosage schedules to provide "full immunization" were comparatively rarely attained, the vaccine appeared to be about 75 per cent effective. Extended and convincing data on this point were provided at the November meeting of the American Public Health Service in a paper entitled "The Surveillance of Poliomyelitis in the United States in 1955" by Alexander Langmuir, M.D., Neal Nathanson, M.D., and William Hall Jackson, Ph.D., of the U. S. Public Health Service Communicable Disease Center, Atlanta, Georgia.

Although the intention of the Massachusetts State Polio Advisory Committee in recommending postponement of a vaccination program in Massachusetts for further study is unquestionably well meaning, it seems equally reasonable to acquaint Massachusetts physicians with the weight of evidence and authority that warrants and encourages vaccination now.

THOMAS M. RIVERS, M.D.
Assistant to the President
National Foundation for Infantile Paralysis
New York City

TOXIC EFFECTS OF PHENYLBUTAZONE

To the Editor: Dr. E. F. Mauer, in his article published in the September 8 issue of the *Journal,* mentioned my views on the influence of age and previous invalidism on the frequency of toxic reactions from phenylbutazone. I still believe that most of the severe reactions that he refers to would have been avoided if the following rules had been observed: the drug should not be given to patients over sixty-five years of age or to those with chronic disorders of blood, alimentary, cardiovascular or urinary system; the dose should not exceed 400 mg. daily (for most patients 300 mg. is sufficient); the drug should be withdrawn as soon as toxic effects appear; and ineffective trials should not last longer than seven days.

In the 23 fatal cases, 8 patients were more than sixty-five years old. One of these had chronic nephritis. Another patient, aged sixty, was obese and an alcoholic, and kept taking the drug for five days after symptoms of gastric ulceration had appeared. Another, aged sixty-four, who had been anemic some time before and had recently had a gold rash, had no hemoglobin estimation before taking phenylbutazone; after he had been a week on 600 mg. daily his nose bled, and a rash appeared; yet he took the drug for a further week — he died of aplastic anemia. Still another patient, aged fifty-nine, who had had chronic bronchitis for years, died of acute lobar pneumonia after taking 400 mg. daily for ten weeks.

Two patients were known to be sensitive to other drugs; 1 took 800 mg. daily for seventeen days and continued for several days after toxic symptoms appeared. In 2 others the drug had been withdrawn for a brief period because of toxic symptoms but was continued after a week. Eight of

those already mentioned took 600 mg. daily or more for more than two weeks. Others took excessive doses as follows: 1200 mg. daily for three days, 1000 mg. for nine days, 600 mg. for forty-two days and 600 mg. for twenty-six days. One of these was not relieved of her pains and took the drug as a placebo. Of another patient, aged forty-four, there are no details of dose or duration of treatment.

Of the remaining 3 patients, the history of 1 suggests that she had taken the drug for many days after toxic symptoms had appeared. Such a history was definite in many cases and implied in others. Persistence in this manner is a common cause of worsening of toxic symptoms that have already appeared. Occasionally, the symptoms progress (as in 1 fatal case), but they usually start to improve as soon as the drug is discontinued. Every patient should be given a list of toxic symptoms and told to stop treatment as soon as any appear.

Thus, in addition to Dr. Mauer's patient, there were only 2 fatal cases in which there were no contraindications and the patients were not given excessive doses. It should also be remembered that nearly all these deaths occurred in 1952 or early in 1953, when the contraindications and the correct dosage were not common knowledge. Of 5 deaths reported during 1954, 1 had occurred in December, 1952, 1 in February, 1953, 1 in June, 1953, and 1 in July, 1953.

If the nonfatal reactions are studied in detail many of the patients are found to have been over age, to have had predisposing disorders, to have taken what are now known to be excessive doses or to have persisted with treatment after toxic symptoms appeared. Dr. Mauer's reminder is necessary lest physicians become unduly complacent.

MICHAEL KELLY

Melbourne, Australia

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Renal Function. Edited by Stanley E. Bradley, M.D., associate professor of medicine, Columbia University College of Physicians and Surgeons. 8°, cloth, 218 pp., with 47 illustrations and 12 tables. New York: Josiah Macy, Jr., Foundation, 1954. $3.75. (Transactions of the Fifth Conference October 14, 15 and 16, 1953, Princeton, N. J.)

The subjects discussed at this conference comprised the nephrotic syndrome and acute renal failure. There is a cumulative index for the years 1949 to 1953 inclusive.

The Development of Personality. By C. G. Jung. Translated by R. F. C. Hull. 8°, cloth, 235 pp. New York: Pantheon Books, Incorporated, 1954. $3.75.

This volume is No. 17 in the collected works of Jung.

Audiologie. Vorträge des ersten Deutschen Audiologenkurses in Freiburg i. Br. vom 5. bis 9. X. 1953. Edited by Prof. Dr. F. Zöllner, director, Univ.-Klinik für Hals-, Nasen- und Ohrenkränke, Freiburg i. Br. 8°, paper, 216 pp., with illustrations. Stuttgart: Georg Thieme, 1954. DM 14.40. (Distributed by Grune and Stratton, New York City.)

This volume forms the transactions of the first congress on audiology, at which 17 papers were read on various aspects of the subject. Lists of references are appended to the articles. The book should be in all collections on otology.

Fortschritte der Tuberkuloseforschung: Advances in Tuberculosis research: Progrès de l'Exploration de la Tuberculose. Volume 6. Edited by Dr. Hans Birkhäuser and Dr. Hubert Bloch. 8°, cloth, 242 pp., with 62 illustrations. New York: S. Karger, 1955. Swiss francs 34.60.

Recent Studies in Bioclimatology: A group. Volume 2, October 1954, No. 8. Edited by F. Sargent, II, and R. G. Stone. With a preface by Jacques M. May. 4°, paper, 121 pp., with illustrations and tables. Boston: American Meteorological Society, 1954.

An Outline of the Treatment of Fractures. By the Committee on Trauma. Fifth edition, revised and amplified. 8°, paper, 93 pp., with 45 illustrations. Chicago: American College of Surgeons, 1954.

Hyperostosis Craniï; Stewart–Morel Syndrome; Metabolic Craniopathy; Morgagni's Syndrome; Stewart–Morel–Moore Syndrome (Ritvo); Le Syndrome de Morgagni–Morel. By Sherwood Moore, M.D. 4°, cloth, 226 pp., with 107 illustrations. Springfield, Illinois: Charles C Thomas, 1955. $10.50.

Christopher's Minor Surgery. Edited by Alton Ochsner, M.D., William Henderson Professor of Surgery and chairman, Department of Surgery, Tulane University of Louisiana School of Medicine; and Michael E. DeBakey, M.D., professor of surgery and chairman, Department of Surgery, Baylor University College of Medicine. 8°, cloth, 547 pp., with 251 illustrations. Philadelphia: W. B. Saunders Company, 1955. $9.00.

Lehrbuch und Atlas der Anatomie des Menschen. By Prof. Dr. Fr. Kopsch, professor-in-ordinary of anatomy, Weiland 2, and direktor, Anatomisches Institut der Humboldt-Universität, Berlin. Band I. *Allgemeines, Skeletsystem, Muskelsystem, Gefässystem.* 19th edition. 4°, cloth, 736 pp., with 731 illustrations. Stuttgart: Georg Thieme, 1955. DM. 64.50. $15.35. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Animal Agents and Vectors of Human Disease. By Ernest Carroll Faust, M.A., Ph.D., William Vincent Professor of Tropical Diseases and Hygiene, and head, Division of Parasitology, Department of Tropical Medicine and Public Health, Tulane University of Louisiana School of Medicine, consultant, Armed Forces Institute of Pathology, and consultant, United States Public Health Service. 8°, cloth, 660 pp., with 216 illustrations and 12 tables. Philadelphia: Lea and Febiger, 1955. $9.75.

Essentials of Medicine: The art and science of medical nursing. By Charles Phillips Emerson, Jr., M.D., associate professor of medicine, Boston University School of Medicine, visiting physician and director of Clinical Laboratories, Hematology Clinic and Radioisotope Division, Massachusetts Memorial Hospitals, consultant in hematology, United States Public Health Service Hospital, Brighton, and attending physician, Veterans Administration Hospital, Boston; and Jane Sherburn Bragdon, R.N., S.B., associate director, School of Nursing, Massachusetts Memorial Hospitals, and clinical assistant in medical and surgical nursing, Boston University School of Nursing. Seventeenth edition. 8°, cloth, 922 pp., with 268 illustrations, including 19 subjects in full color. Philadelphia: J. B. Lippincott Company, 1955. $4.75.

Die Bronchographie. By Dr. Ernst Stutz, lecturer, Universität Freiburg I. Br.; and Dr. Heinz Vieten, lecturer, Medizinische Akademie, Düsseldorf. 4°, cloth, 250 pp., with 181 illustrations. Stuttgart: Georg Thieme, 1955. DM66.- $15.70. DM 59.40.- $14.15. (Distributed in America by the Intercontinental Medical Book Corporation, New York City.)

Correlative Neurosurgery. By Edgar A. Kahn, M.D., Robert C. Bassett, M.D., Richard C. Schneider, M.D., and Elizabeth Caroline Crosby, Ph.D., M.D. With a foreword by Kenneth G. McKenzie, M.B., Toronto, F.R.C.S. (C), consulting senior surgeon to the Toronto General Hospital. 4°, cloth, 413 pp., with 235 illustrations and 8 tables. Springfield, Illinois: Charles C Thomas, 1954. $19.50.

Prepayment and the Community. (Financing Hospital Care in the United States. Volume 2.) Edited by Harry Becker. 8°, cloth, 356 pp., with 86 charts and 72 tables. New York: McGraw-Hill Book Company, Incorporated, 1955. $4.50.

Financing Hospital Care for Nonwage and Low-Income Groups. (Financing Hospital Care in the United States. Volume 3.) Edited by Harry Becker. 8°, cloth, 110 pp., with 23 charts and 25 tables. New York: McGraw-Hill Book Company, Incorporated, 1955. $2.50.

The Technique of Psycho-Analysis. By Edward Glover, M.D. 8°, cloth, 404 pp. New York: International Universities Press, 1955. $7.50.

Advances in Pediatrics. Volume 7. Edited by S. Z. Levine, M.D., Cornell University Medical College. 8°, cloth, 351 pp., with illustrations, plates and tables. Chicago: Year Book Publishers, Incorporated, 1955. $8.00.

The Abnormal Pneumoencephalogram. By Leo M. Davidoff, M.D., professor of surgery and chairman, Department of Surgery, Albert Einstein College of Medicine, director of surgery, Bronx Municipal Hospital Center, and chief of neurosurgery, Mount Sinai Hospital; and Bernard S. Epstein, M.D., chief, Department of Radiology, Long Island Jewish Hospital, New Hyde Park, New York. Second edition. 4°, cloth, 518 pp., with 696 illustrations. Philadelphia: Lea and Febiger, 1955. $15.00.

A Textbook of Physiology. Edited by John F. Fulton, M.D., Sterling Professor of the History of Medicine, Yale University School of Medicine. Seventeenth edition. 8°, cloth, 1275 pp., with 599 illustrations with 66 tables. Philadelphia: W. B. Saunders Company, 1955. $13.50.

Introduction to Thermodynamics of Irreversible Processes. By I. Prigogine, D.Sc., professor, Faculty of Science, University of Brussels. 8°, cloth, 115 pp., with illustrations. Springfield, Illinois: Charles C Thomas, 1955. $4.75. (Publication No. 185, *American Lecture Series.*)

Die Cytologie des Bronchialsekretes. By Dr. Med. P. Hartmann, assistant, Pathologisches Institut der Medizinischen Akademie Düsseldorf. 8°, paper, 110 pp., with 68 illustrations and 2 tables. Stuttgart: Georg Thieme, 1955. DM 24.- $5.70. (Distributed by Intercontinental Medical Book Corporation, New York City.)

The Pharmacological Basis of Therapeutics: A textbook of pharmacology, toxicology, and therapeutics for physicians and medical students. By Louis S. Goodman, M.A., M.D., professor of pharmacology, University of Utah College of Medicine; and Alfred Gilman, Ph.D., professor of pharmacology, Columbia University College of Physicians and Surgeons. Second edition. 4°, cloth, 1831 pp., with 89 illustrations and 72 tables. New York: Macmillan, 1955. $17.50.

Segmental Anatomy of the Lungs: A study of the patterns of the segmental bronchi and related pulmonary vessels. By Edward A. Boyden, Ph.D. (Med. Sc.). 4°, cloth, 276 pp., with 125 illustrations, 37 tables and 12 colored plates. New York: Blakiston Division, McGraw-Hill Book Company, Incorporated, 1955. $15.00.

The Joints of the Extremities: A radiographic study. Notes of non-routine methods, non-routine ideas, and less-common pathology. By Raymond W. Lewis, M.D. 4°, cloth, 108 pp., with 102 illustrations. Springfield, Illinois: Charles C Thomas, 1955. $8.50.

The Human Machine: Biological science for the Armed Services. By Charles W. Shilling, captain, Medical Corps, United States Navy. 4°, cloth, 292 pp., with 156 illustrations and 28 tables. Annapolis: United States Naval Institute, 1955. $5.00.

Ion Exchange and Adsorption Agents in Medicine: The concept of intestinal bionomics. By Gustav J. Martin, Sc.D., research director, National Drug Company, Philadelphia. 8°, cloth, 333 pp., with 15 line drawings, 11 photographs and 49 tables. Boston: Little, Brown and Company, 1955. $7.50.

The Laboratory Diagnosis of Cancer of the Prostate. Edited by F. Homburger and W. H. Fishman, Ph.D. 8°, paper, 51 pp., with 13 figures and 7 tables. Boston: Tufts College Medical School, 1954. (Distributed by Brown and Connolly, Incorporated, Boston.) $2.00.

NOTICES

AMERICAN COLLEGE OF CHEST PHYSICIANS AND THE OVERHOLT THORACIC CLINIC

There will be a combined meeting of the New England States Chapter of the American College of Chest Physicians and the Overholt Thoracic Clinic in the Joslin Auditorium of the New England Deaconess Hospital, Boston, on Wednesday, January 18, at 4 p.m.

Dr. Andre Cournand will give a talk entitled "The Physiological Basis of the Treatment of Chronic Pulmonary Emphysema."

SOUTH END MEDICAL CLUB

A meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, January 17, at 12 noon. Dr. Sidney Farber will speak on the subject "Chemotherapy of Cancer." All physicians are invited.

BOSTON CITY HOSPITAL HAND SERVICE

The Hand Service of the Boston City Hospital will present a symposium on hand surgery at the Dowling Amphitheater, Boston City Hospital, on Friday afternoon and evening, January 20. The program is as follows:

2-5 o'clock (Dr. Michael L. Mason will discuss each paper):

Pasteurella Infections of the Hand. Dr. John J. Byrne.

Tumors of the Hand. Dr. John C. Crandon.
Arterial Trauma to the Upper Extremity. Dr. Donald C. Nabseth.
Peripheral-Nerve Trauma to the Upper Extremity. Dr. William F. Flynn.
Tendon Transfer after Trauma to Median, Ulnar and Radial Nerves. Dr. J. Edward Flynn.
8 o'clock:
Dupuytren's Contracture. (Fourth Annual Harrison E. Kennard Lecture.) Dr. Michael L. Mason.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

The thirty-third annual meeting of the American Orthopsychiatric Association, Incorporated, will be held at the Hotels Commodore and Roosevelt, New York City, March 15-17, 1956. Orthopsychiatric theory and practice in five broad fields will be covered by representatives of the wide range of professional disciplines and settings practicing in the field of orthopsychiatry. These fields include schools and mental health, inpatient and outpatient psychiatric treatment of children, adolescence and juvenile delinquency, psychiatric-clinic management and adult psychotherapy. Further information may be obtained from Dr. Marion F. Langer, American Orthopsychiatric Association, 1790 Broadway, New York 19, New York.

INTERNATIONAL ACADEMY OF PROCTOLOGY

The eighth annual teaching seminar of the International Academy of Proctology will be held at the Drake Hotel, Chicago, April 23-26. International, national and local program committees are planning the seminar on anorectal and colonic surgery. Special entertainment has been planned for the delegates and trustees and their wives. All physicians and their wives are invited to attend, whether or not they are affiliated with the Academy.

SOCIETY MEETINGS AND CONFERENCES

JANUARY 12–14. Pan American Congress of Ophthalmology. Page 944, issue of November 24.
JANUARY 12–26. Consultation Clinics for Crippled Children in Massachusetts. Page 1177, issue of December 29.
JANUARY 13, 20 and 27 and FEBRUARY 3. Yale University School of Medicine, Yale-New Haven Medical Center. Page 1092, issue of December 15.
JANUARY 16. Hartford Medical Society. Page 708, issue of October 20.
JANUARY 16, FEBRUARY 6, MARCH 5 and APRIL 2. Fried Lecture Series. Page 535, issue of September 22.
JANUARY 17. South End Medical Club. Page 85.
JANUARY 18. American College of Chest Physicians and the Overholt Thoracic Clinic. Page 85.
JANUARY 20. Boston City Hospital Hand Service. Page 85.
JANUARY 20–27. Fifth Panamerican Congress of Gastroenterology. Page 746, issue of October 27.
JANUARY 23. Boston Committee on Alcoholism. Page 44, issue of January 5.
JANUARY 25, FEBRUARY 29, MARCH 21 and APRIL 25. Massachusetts Heart Association. Page 623, issue of October 6.
JANUARY 25, MARCH 21 and APRIL 26. Phi Delta Epsilon Fraternity Graduate Club Program. Page 118, issue of July 21.
JANUARY 30–FEBRUARY 8, MARCH 19–28 and JUNE 4–13. Army Medical Service Postgraduate Course. Page 84, issue of July 14.
FEBRUARY 13–16. American College of Surgeons. Page 1136, issue of December 22.
FEBRUARY 14. Harvard Medical Society. Page 44, issue of January 5.
FEBRUARY 15, MARCH 28 and APRIL 18. Greater Boston Medical Society. Page 208, issue of August 4.
FEBRUARY 20–22. Atlanta Graduate Medical Assembly. Page 1136, issue of December 22.
MARCH 15–17. American Orthopsychiatric Association. Notice above.
MARCH 19–22. American Academy of General Practice. Page 1092, issue of December 15.
MARCH 24 and 25. American Psychosomatic Society. Page 260, issue of August 11.
APRIL 23–26. International Academy of Proctology. Notice above.
MAY 2. Postgraduate Medical Institute. Page 487, issue of September 15.
MAY 3–5. American Goiter Association. Page 348, issue of August 25.
MAY 28–JUNE 1. European Symposium on Vitamin B. Page 578, issue of September 22.
JUNE 21–23. Society of Nuclear Medicine. Page 1092, issue of December 15.
JUNE 21–24. American Academy of Dental Medicine. Page 994, issue of December 1.
AUGUST 19–23. American College of Chest Physicians. Page 840, issue of November 10.
SEPTEMBER 10–14. American Dietetic Association. Page 1180, issue of December 29.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, JANUARY 19

THURSDAY, JANUARY 19
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Yamins A, Beth Israel Hospital.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Guest Speaker of the Bingham Associates. Acute and Chronic Renal Failure. Dr. Richard Porter. Cape Cod Hospital, Hyannis, Massachusetts.
11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*11:15 a.m. Thoracic Conference. Pulmonary Vascular Disease. Dr. Lewis Dexter. Main Amphitheater, Peter Bent Brigham Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Staff Conference. Some Basic and Clinical Developments in Coagulation. Dr. Benjamin Alexander. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Tumor Clinic. Dr. T. W. Botsford. Amphitheater, Peter Bent Brigham Hospital.

FRIDAY, JANUARY 20
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*1:00–3:00 p.m. Combined Medical-Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
2:00–5:00 p.m. Boston City Hospital Hand Service. Dowling Amphitheater, Boston City Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, JANUARY 21
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Benjamin Etsten, Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
*11:00 a.m.–12:00 m. Hematology Conference (Blood Clinic). Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, JANUARY 23
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry, By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Medical-Pathological Conference. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

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